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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 39 FEBRUARY, 1956 NO. 2

Original Communications

THE HEMODYNAMICS OF DECHOLIN SODIUM IN SHOCK

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(From the Departments of Surgery and Pharmacology, Baylor University College of Medicine)

WE RECENTLY observed that the intravenous injection of Decholin sodium[1] during hemorrhagic shock was associated with an increase in survival rate. This stimulated our interest to study further its pharmacologic effect. Our findings in both intact animals and those in hemorrhagic shock showed that when given intra-arterially Decholin sodium has a primary vasodilating action, and when given into the femoral vein it is associated with a temporary drop in arterial pressure, a temporary increase in cardiac output, and a sustained increase in arterial blood flow to the liver. An increase in hepatic arterial flow also occurred when it was injected into the hepatic artery or splenic vein. A 20 per cent solution of Decholin Sodium (200 mg. per c.c.) was used throughout the experiments.

METHODS

The experiments were performed on dogs of from 10 to 15 kilograms in weight. An air-conditioned room was used in which the temperature was 26° C. with occasional variations of 2° to 5°. The instruments, tubing, cannulas, flowmeters, and so on, were clean but not sterile. A helial flowmeter similar to the one described by Bruner[2] was used to determine the hepatic arterial flow. The flowmeter had a volume of 3 c.c. and a 0.25 c.c. air bubble was used in making the determinations. The cardiac outputs were determined by the pressure pulse methods of Hamilton and Remington[3] and the total peripheral resistance was calculated by the use of the formula $\frac{PM - 20}{c.c./sec.}$. The blood flow of the femoral artery was ascertained with a rotameter as described by Gregg and Shipley.[4] A water manometer was used to record the pressures in the femoral splenic veins and the right auricle.

Venous Pressure.—The effect of Decholin sodium, via the femoral vein, on the right auricle, femoral, and splenic vein pressures was ascertained on 30 occasions. No effect was noted on the right auricle or femoral vein pressure. The splenic vein pressure increased (0.5 to 1.0 mm.) slightly on 9 occasions, decreased (0.5 to 1.0 mm.) in 16 and there was no change in 5.

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Hepatic Arterial Flow.—As a control, the hepatic arterial flow was ascertained in 5 intact animals and in 7 animals in hemorrhagic shock. A minimum flow of 270 c.c. and a maximum of 300 c.c. per minute was obtained in the intact animals. The hepatic arterial flow averaged 5.2 c.c. per one minute on the 7 animals in hemorrhagic shock when the mean arterial pressure was 30 mm. Hg. The effect of intravenous (1 c.c. into femoral vein) Decholin sodium on arterial flow was ascertained 17 times on 7 dogs in hemorrhagic shock (arterial pressure 30 mm. Hg). The proximal and distal ends of the hepatic artery were connected through the flowmeter for 3 determinations and the proximal end of the femoral artery was substituted for the proximal hepatic artery on 4 occasions. No difference could be seen between using the proximal ends of the hepatic or femoral arteries as a source of blood. There was an increase in blood flow following the administration of Decholin sodium into the femoral

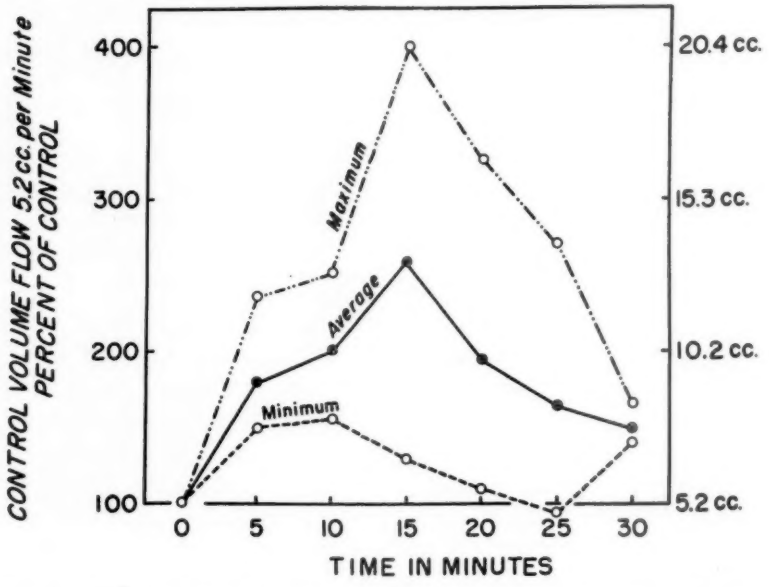

Fig. 1.—Hepatic arterial blood flow after i.v. injection of sodium dehydrocholate (systemic arterial pressure 30 mm. Hg).

veins on 15 occasions by at least 50 per cent of the control level and no effect in 2 instances. The greatest increase in hepatic arterial flow occurred about fifteen minutes after the injection and averaged 256 per cent of the control. The average flow thirty minutes after injection was still 55 per cent above the control and usually returned to the control level thirty-five to forty-five minutes after the injection (Fig. 1). In the 2 instances in which there was no increase in the hepatic arterial flow the animals had been in shock sufficiently long to be classed as irreversible by criteria previously described[1] and were not, therefore, included in Fig. 1. The effect on hepatic arterial flow during hemorrhagic shock after 1 to 2 c.c. of Decholin sodium was injected into the hepatic artery was ascertained 14 times. There was an increase in 13 instances, usually within two minutes, of 200 to 400 per cent of the control level and a return to control levels in from twelve to twenty minutes. There was no change on 1 occasion. The animal in which no change occurred could be classified as in irreversible shock[1] and expired within ten minutes.

Femoral Arterial Flow.—When small amounts (.25 to 1.0 c.c.) of Decholin sodium are injected intra-arterially (Table I) into a femoral artery, there is an immediate increase in blood flow through this vessel, indicating that Decholin sodium has a primary vasodilating action.

TABLE I. EFFECT OF DECHOLIN SODIUM ON BLOOD FLOW IN THE FEMORAL ARTERY WHEN INJECTED INTRA-ARTERIALLY

C.C. DOG LSH 7. PM 102 MM. HG	FLOW/C.C. SEC.	C.C. DOG LS 8. HEMORRHAGED DOG 15 KG. ARTERIAL PM 50 MM. HG	FLOW/C.C. SEC.
Control	0.75	Control	3.42
Decholin sodium 0.2	0.88	Decholin sodium 0.5	5.10
Control	0.60	Control (after 300 c.c.)	1.30
Decholin sodium 0.5	1.97	Decholin sodium 0.5	2.23
Control	0.63	Control	1.52
Decholin sodium 0.5	1.65	Control (saline at pH 9.0)	1.57
Control	0.66		
Control (saline at pH 9.0)	0.69		

Cardiac Output and Peripheral Resistance.—On injection of varying amounts (.25 to 3.0 c.c.) of Decholin sodium intravenously into both normal and shock dogs, the cardiac output increased and the systolic and diastolic pressures and peripheral resistance decreased (Table II).

TABLE II. EFFECT OF DECHOLIN SODIUM ON CARDIAC OUTPUT AND PERIPHERAL RESISTANCE WHEN ADMINISTERED VIA FEMORAL VEIN

AMOUNT C.C.	S/D*	PM†	C.O./C.C. SEC.‡	R_p§
Hemorrhaged Dog F. V. 22				
Control	132/86	106.7	78	1.11
Control hem. 300 c.c.	44/28	35.2	17	0.78
Decholin sodium 1.0 c.c.	44/24	33	29	0.45
Control	42/24	32	24	0.50
Decholin sodium 2.5 c.c.	48/22	33	33	0.41
Control Dog—No Hemorrhage F. V. 10				
Control	148/78	109	43	2.04
Decholin sodium 0.2 c.c.	150/86	114	58	1.61
Control	152/96	121	34	3.00
Decholin sodium 0.5 c.c.	126/72	93	59	0.60
Control	140/76	105	52	1.62
Saline (pH 9.0)	144/78	107	54	1.62

*Systolic and diastolic.
†Mean pressure.
‡Cardiac output.
§Peripheral resistance.

DISCUSSION

From our previous experiences,[5] and those of others,[6] an increase of arterial blood flow to the liver, or the administration of oxygen or blood into the splenic vein lowers the mortality rate of shocked dogs. Schwiegk[7] and Grodins[8] demonstrated that Decholin sodium increases the hepatic arterial flow, and we verified their findings with a bubble flowmeter. Neither the instrument (thermostromuhr) used by them or the bubble flowmeter is without technical error. However, the consistent demonstration of an increase in hepatic arterial flow by 3 independent groups indicates that its percentage of occurrence is probably high. The increase in hepatic arterial flow associated

with the administration of Decholin sodium is small (50 per cent). However, recent work on ligation of the hepatic artery both in human beings and experimental animals indicates that even a small increase in hepatic arterial flow is

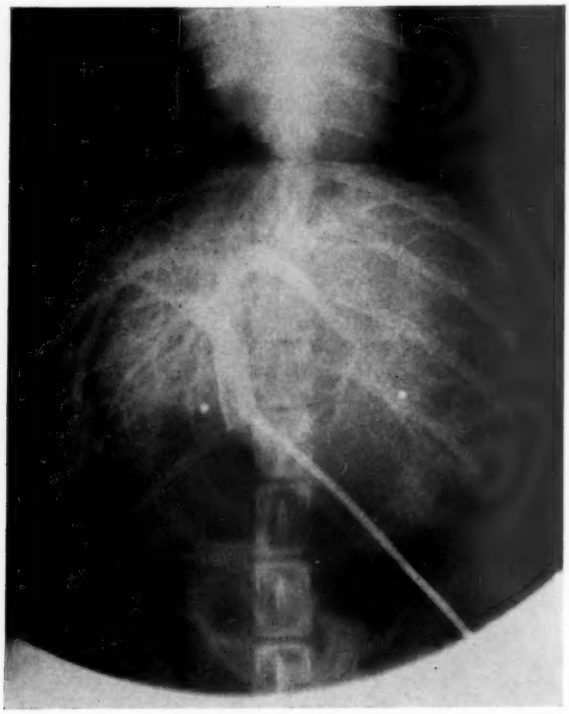

Fig. 2.—Thoratrast demonstration of the size of portal vein before shock.

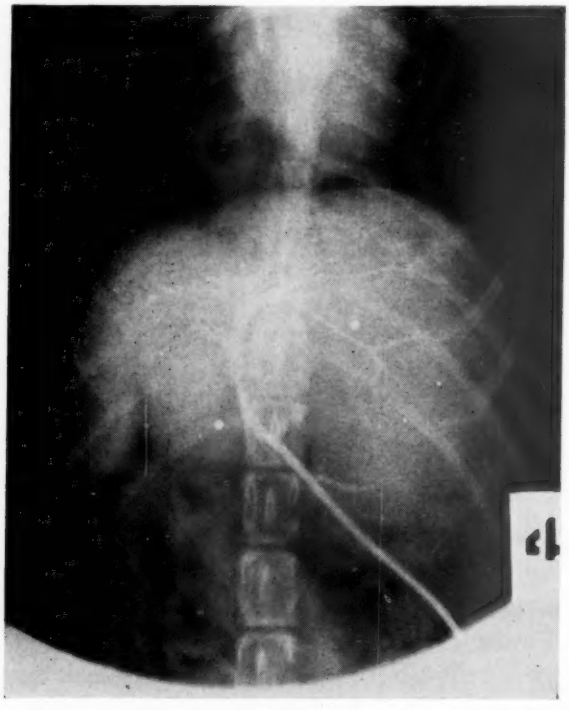

Fig. 3.—Thoratrast demonstration of the decrease in size of portal vein during shock.

significant in survival.[5] Previous experience of one of us[1] with intravenous Decholin sodium in shocked dogs showed it to be associated with a survival rate of 75 per cent as compared with 22.3 per cent in controls. Therefore, even though the increase in hepatic arterial flow observed after administration of Decholin sodium is small, it is possibly significant. This increase in hepatic arterial flow could not be accounted for on the changes in cardiac output, venous pressure, or the use of different afferent vessels in the flowmeter, so that it seems very possible that it is associated with a vasodilation of the intrahepatic portion of the hepatic artery. The demonstration of the primary vasodilating action of Decholin sodium on the femoral artery supports this view.

The decrease in size of the portal vein during shock can be demonstrated with the use of Thoratrast (Figs. 2 and 3), but the small change in size in the hepatic artery associated with the administration of blood or Decholin sodium could not be demonstrated by this method.

The intravenous administration of Decholin sodium has several possible clinical uses. One is for military use in those areas forward of blood stations, for treatment by civilian first-aid teams on the way to the hospital, and to prevent irreversible changes in the liver during operations where it is desirable for the arterial pressure to be extremely low. From our experience, it would appear that to be effective administration will have to begin early before irreversible changes occur.

SUMMARY

In both intact animals and those in hemorrhagic shock we have found that Decholin sodium (A) when given intra-arterially had a primary vasodilating action; (B) when given into the femoral vein was associated with a temporary drop in arterial pressure, temporary increase in cardiac output, and a sustained increase in arterial blood flow to the liver; and (C) the increase in hepatic arterial flow also occurred when it was given into the hepatic artery or splenic vein.

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CANCER OF THE STOMACH

An Analysis of 1,152 Cases

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SURGEONS who undertake the treatment of patients with cancer of the stomach are obliged to make every effort to cure as many patients as possible and at the same time to offer a maximum of life and comfort to those who are found incurable. This would be a simple problem if all patients could be classified as curable or incurable when first seen. At the present time, unfortunately, this is not possible. The presence or absence of lymph node involvement has three to four times the influence on the ultimate five-year survival rate as does the proficiency of the surgeon.

To those engaged in attempting to improve the over-all results in gastric cancer, it is essential to keep in mind the four ever-present factors which govern the outcome of this disease: (1) the part played by the disease; (2) the part played by the patient; (3) that of his personal physician; and (4) the role of the surgeon. From the onset of the disease until definitive treatment is afforded, two events are simultaneously taking place: the growth and spread of the tumor, on the one hand, and the series of events which lead to its recognition and treatment. These two events, although occurring simultaneously, are not progressing at the same rate. We have no control over the progression of the disease, but the disease, to a great extent, controls the speed with which the medical profession discovers its presence and undertakes its treatment.

It is necessary, therefore, to keep in mind that there are a certain number of patients whose disease is rapidly progressing and can never be cured by surgery, regardless of how quickly it is undertaken. In contradistinction, there are other patients whose tumors progress slowly and metastasize late who can be cured even after a long delay in the onset of treatment.

With this perspective kept in mind, it is the purpose of this paper to present the total experience of the University of Minnesota Hospitals with cancer of the stomach, in an attempt to assess the accomplishment and to evaluate the prognostic factors which bear on the outcome.

During the fourteen-year period from Jan. 1, 1936, to Jan. 1, 1950, a total of 1,201 cases of cancer of the stomach were seen at this hospital. This includes all outpatients as well as those admitted to the hospital. Forty-nine patients refused surgical intervention or failed to return for final disposition. This is a

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report of the 1,152 patients remaining, of which 934 had the diagnosis established by microscopic verification or at operation. This includes 6 cases of lymphosarcoma, 3 patients with leiomyosarcoma, and the remaining 925 cases, diagnosed as carcinoma.

SEX INCIDENCE AND AGE

Sex and age incidence are presented in Fig. 1: 853 (74.0 per cent) were men and 299 (26.0 per cent) of the 1,152 patients were women. This closely parallels the sex incidence of five-year survivors in this series, namely, 73.4 per cent men and 26.6 per cent women. This threefold greater incidence in men is somewhat higher than that reported by Jemerin and Colp,[15] and Pack and McNeer,[21] but is similar to the reports of Berkson and associates[3] and other investigators.[21, 24] Except for the period 1939 to 1941, the male:female ratio of 3:1 has been constant.

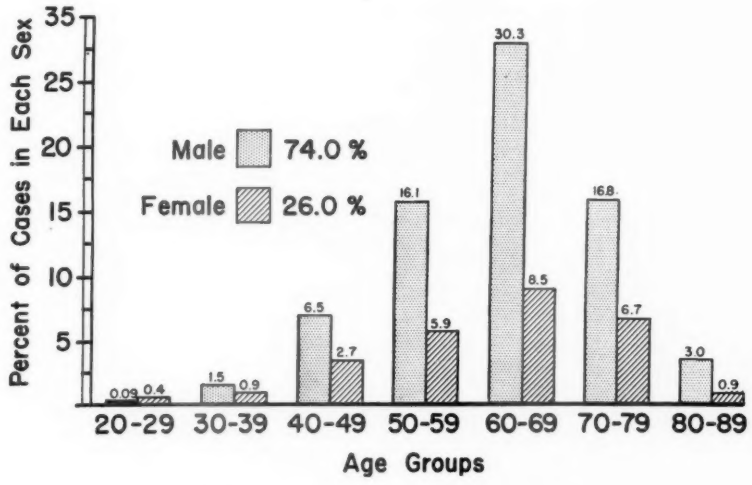

Fig. 1.—Age and sex distribution.

The average age of all patients was 62.8 years and the median age 65 years. The average age of all men was 63.1 years, of women 61.8 years, and the median ages 65 years and 63 years, respectively. The youngest patient was 24 years, the oldest, 89 years; 84.3 per cent of all patients were in the age group between 50 to 79 years; 62.3 per cent were from 60 to 79 years of age; and 38.8 per cent were in the seventh decade of life. A definite increase in age had occurred from 1936 to 1949. The average ages of all cases, of men, and of women, in 1936 was 60.2, 61.0, and 57.4 years, respectively, as compared with 1949, when a rise to 64.8, 64.5, and 74.6 years, respectively, was noted. The average age of this group is approximately 5 to 10 years higher than those reported by others.[3, 17, 20, 26]

It is generally considered that malignant disease in old age is a slowly progressing one, as compared with that in the younger age group. The success in curing these patients may be offset by the higher morbidity and mortality following gastric resection, especially with the ever-present malnutrition, inanition, and associated cardiorespiratory disease found in the older age group.

DIAGNOSIS

The need for greater effort in diagnosing the disease early is evident when one reviews the average duration of symptoms in patients treated between 1936 and 1949, as presented in Table I. The third column of figures, illustrating delay in diagnosis, includes many cases in which only the time from onset of symptoms to surgery is known. Included in the averages presented in Table I are many patients with "ulcer" symptoms of very long duration which, therefore, will affect the average duration to a very great extent. The median duration of delay has much greater significance and is a more accurate interpretation of our findings. Other investigators[16, 17] have reported average delays from onset of symptoms to surgical evaluation ranging from fifteen to nineteen months.

There is evidence to suggest that in many instances gastric cancer is a relatively slow-growing disease with a long "silent interval." Friesen[12] noted that in those cases in which cancer was left in the line of resection at time of gastrectomy, there was an average period of twenty months prior to the recurrence of symptoms. Thus, from the data presented in Table I, it appears that patients were not reporting to their doctor any sooner and that the physicians were not diagnosing gastric cancer and getting the patients to surgery any more quickly in 1949 than fourteen years earlier. The reasons for this are not entirely apparent. The frequent statements expressed by physicians that they have never seen a five-year survivor from gastrectomy for cancer of the stomach, or the applicable truism of Pack,[22] that "simple indigestion is

TABLE I. BREAKDOWN OF DELAY

ALL CASES (YEARS)	AVERAGE MEDIAN (MONTHS)		
	ONSET TO MD*	MD TO SURGERY*	ONSET TO SURGERY
1936-38	6.4	5.2	14.0
	2.0	4.0	8.0
1939-41	5.2	4.9	14.8
	3.0	4.0	6.0
1942-44	9.5	7.5	13.6
	2.0	2.0	5.0
1945-47	7.1	6.3	17.6
	2.0	2.0	7.0
1948-49	4.5	7.5	18.4
	2.0	3.0	6.0
1936-49	6.8	6.3	15.8
	2.0	3.0	6.0
5-year survivals 1936-49	7.8†	12.2†	26.8
	3.0	3.0	12.0

*58.3 per cent of cases.
†78.9 per cent of cases.

probably the most dangerous complaint of any person in middle or late life. Because it is the most common, little attention is paid to the vague but portentous beginnings of what may prove to be a fatal disease," are sufficient evidence for the persistent lack of improvement in the delay period before surgery is invoked. Thus, any improvement in the five-year survival during the fourteen-year period presented appears to be a direct result of improvement in surgical therapy. Jemerin and Colp[15] similarly have shown no decrease in delay before diagnosis

and treatment during the years 1938 to 1947. The interval between onset of symptoms and institution of therapy was less than three months in 24 per cent of their patients. Boyce,[4, 5] Harvey and co-workers,[14] and Welch and Allen[32] have reported similar findings, somewhat contrary to what was expected.

From the data presented in Table II, 29.2 per cent of the patients presented themselves for surgical consultation within three months and 52.4 per cent of the patients in our study were afforded surgical consultation within six months after the onset of symptoms. Over 10 per cent of the patients presented symptoms of over two years' duration before a diagnosis of cancer of the stomach was made and surgical consultation requested. This group consisted of patients with long "ulcer" histories ranging from two to forty years. Many in this group had been previously treated with ulcer diet and antacids with excellent relief of symptoms during the earlier years of their difficulties. It was only when relief of symptoms could not be obtained by the aforementioned means that surgical consultation was recommended.

TABLE II. PER CENT BREAKDOWN OF DURATION OF SYMPTOMS IN MONTHS

	PER CENT CASES				
ALL CASES (YEARS)	0-3 MO.	4-6 MO.	7-12 MO.	13-24 MO.	OVER 24 MO.
1936-38	27.0	19.1	28.1	16.3	9.5
1939-41	26.1	31.0	25.2	8.2	9.5
1942-44	32.3	22.1	27.0	12.8	5.8
1945-47	29.7	19.4	24.5	13.0	13.4
1948-49	31.0	25.1	21.9	8.1	13.9
1936-49	29.2	23.2	25.3	11.7	10.6
5-year survivors 1936-49	18.3	22.0	23.8	16.6	19.3

Ladue and associates[16] have reported 6.2 per cent of the patients in their series were in this group. Ekström[9] has reported that 25 per cent of the patients with gastric cancer present a long history of gastric pain. Lawton and co-workers[17] had noted that 30 per cent of patients with gastric cancer had followed an ulcer regimen at some time, with 78 per cent of these patients having obtained relief of pain.

No significant increase in the percentage of early cases (0 to 6 months) has been noted since 1936.

Only 40.3 per cent of five-year survivors had symptoms for six months or less prior to gastric resection. In addition, 19.3 per cent had symptoms of over 2 years' duration. Thus, it may be presumed that a greater number of slow-growing and late metastasizing gastric cancers are included in the five-year survivals, as compared to the over-all incidence.

SYMPTOMS

Pain is still the most frequent presenting symptom. No attempt was made to present statistically the incidence of all symptoms since, in the natural course of the disease, it is generally known and has been reported that the symptoms of pain, weakness, anorexia, fullness, vomiting, and weight loss are most predominant.[8, 15, 17]

In Table III, the incidence of first symptoms is presented in an attempt to arrive at a means of early identification of this disease. In over 50 per cent of patients, pain was the most common complaint. This pain is characterized in many ways: distressed feeling, indigestion, burning sensation, heartburn, a gnawing or hunger pain, or definite upper abdominal pain, severe in nature, which may or may not be relieved by the ingestion of food.

Cancer of the stomach has no greater ally than the physician who pays little heed to this complaint by procrastination and delay in the early investigation of the patient's symptoms, and "buries the cancer under a mound of powder."[11]

From the data presented in Table III, the presenting symptoms of pain, weakness, anorexia, and fullness were noted in approximately 90 per cent of the patients studied. Less than 1 per cent of the patients in this series had symptoms of far-advanced disease such as dyspnea, abdominal swelling, vertigo, and leg edema when first seen at this hospital. Slightly over 1 per cent of the patients in this group were asymptomatic. This small group consisted of, primarily, those patients with pernicious anemia or those discovered in the Cancer Detection Center by periodic observation of the precursor-achlorhydric group.

TABLE III. FIRST SYMPTOMS, 1,152 CASES

SYMPTOM	PER CENT	SYMPTOM	PER CENT
Pain	51.1	Nausea	1.3
Weakness	10.1	Constipation	1.3
Anorexia	10.1	Diarrhea	0.8
Fullness	8.5	Hematemesis	0.8
Vomiting	3.9	Melena	0.7
Dysphagia	3.4	Regurgitation	0.5
Weight loss	2.8	Dyspnea	0.2
Belching	1.6	Abdominal swelling	0.1
Gas	1.5	Vertigo	0.1
No symptoms	1.3	Leg edema	0.1

There is little evidence to suggest any "typical" syndrome with regard to cancer of the stomach. The physician who is first confronted with the problem must rely upon his clinical experience and diagnostic acumen, rather than "words in the book" in the investigation of this disease. An alert clinician who is cancer-conscious still remains the patient's best friend and benefactor in combating this disease.

Hematemesis, a symptom frequently associated with gastric pathology, was noted in only 11.2 per cent of cases. Others[16] have reported similar figures. The physical signs of cancer of the stomach are of little aid in the early diagnosis of the disease.

LABORATORY STUDIES

Anemia.—Laboratory studies indicative of anemia were noted in 45.1 per cent of 977 patients in whom hemoglobin determinations were made when the patient was first seen at this hospital. Anemia, in this group, includes all patients with hemoglobin values below 11.0 Gm. Jemerin and Colp[15] have reported a 76 per cent incidence of anemia in their series of 344 cases. Others[10, 17]

have reported lower percentages of cases with associated anemia. In the majority of cases in our study, the anemia was primarily of the normochromic or hypochromic variety.

Although anemias are frequently associated with other diseases, either neoplastic or nonneoplastic, the discovery of an anemia in patients presenting gastrointestinal symptoms should not be too lightly dismissed with the promiscuous prescription of iron and liver injections, as is so frequently done. The average American diet is certainly not so deficient in iron as to result in an iron-deficiency anemia. It is generally accepted that iron is reutilized with very little fecal excretion. Therefore, the iron-deficiency anemias seen in patients with cancer of the stomach are mainly the result of continuous leakage of blood into the gastrointestinal tract or, less likely, are secondary to anorexia and weight loss that is so commonly found in gastric cancer patients.

Stool Examination.—Seven hundred and twenty-six patients were examined for occult blood in the stool, employing the guaiac test. Only the results of the guaiac test rather than the benzidine test are reported due to the marked sensitivity of the latter, leading to many false positive readings. Of the patients tested for occult blood in the stool, 83.2 per cent were found to be positive as noted in Table IV. Lawton and associates,[17] employing the benzidine test, reported positive occult blood in the feces in 95 per cent of his cases. Jemerin and Colp[15] have reported an incidence of 71 per cent of patients with gastric cancer exhibiting guaiac positive stools.

TABLE IV. INCIDENCE OF OCCULT BLOOD

	NO. CASES	PER CENT
Stool pos. for blood	607	83.2
Stool neg. for blood	119	16.8
Totals	726	100.0

Although many conditions other than gastric cancer may present themselves by evidencing gastrointestinal bleeding, the postulation[31] that the earliest sign of gastrointestinal cancer is the insidious minute bleeding that occurs due to mucosal alteration by the "microscopic" neoplasm appears to be well founded. Since the median duration of symptoms in the group presented is six months, there is little evidence to suggest that the high incidence of gastrointestinal bleeding noted in this series is of diagnostic significance in the early case of gastric cancer.

Gastric Acidity.—Quantitative determinations of free hydrochloric acid in gastric contents were made in 897 patients. Triple histamine injection was employed in the majority of cases. In Table V it is noted that 650 patients (72.5 per cent) were found to be achlorhydric and 137 (15.3 per cent) hypochlorhydric (less than 30 degrees free hydrochloric acid). Thus 87.8 per cent of all patients examined were either achlorhydric or hypochlorhydric. This high incidence coincides with reports of others.[8, 15, 17]

Although Vanzant and associates[29] have reported that 23 to 28 per cent of the population at age 60 years are achlorhydric and that the percentage in-

creases with advancing age, this figure of almost 90 per cent of patients with gastric cancer exhibiting achlorhydria or hypochlorhydria can be interpreted as being of definite diagnostic significance, in addition to exhibiting a precursor tendency for this disease.

Niazi and co-workers,[19] in 1949, showed that achlorhydria and hypochlorhydria occurs significantly more frequently in patients with cancer of the stomach than in those with extragastric malignancies. They reported achlorhydria and hypochlorhydria to be present in 32.8 per cent and 24.6 per cent, respectively, of patients with extragastric malignancies as compared with 85 per cent and 5 per cent, respectively, in those patients with cancer of the stomach. The high incidence of achlorhydria and hypochlorhydria noted in this series of patients with gastric cancer demonstrates the importance of this test in the diagnosis of cancer of the stomach.

TABLE V. ACIDITY IN 897 CASES IN WHICH DETERMINATION WAS MADE

	NUMBER OF CASES	PER CENT
Achlorhydria	650	72.5
Hypochlorhydria	137	15.3
Normal or hyperchlorhydria	110	12.2
Totals	897	100.0

Gastric analysis is performed in all patients seen in the Cancer Detection Center of this hospital. All those found to be in the achlorhydric-hypochlorhydric group are carefully observed at frequent intervals for signs of gastric cancer. State and associates[27] reported a study of 1,540 patients with achlorhydria or hypochlorhydria followed periodically by roentgenologic examination at the University of Minnesota Hospital Cancer Detection Center, in which 10 were found to have cancer of the stomach. Three of these cases were missed through error in x-ray diagnosis.

Roentgen Examination.—Roentgen examination of the stomach employing the barium meal is still the best means of detecting gastric cancer.[15, 17, 20] Such an examination should include fluoroscopy and spot films, especially with regard to the diagnosis of the early case of gastric cancer.[25]

In a series of 861 patients studied from Jan. 1, 1939, to Jan. 1, 1951, who underwent roentgen or fluoroscopic examination of the stomach, 72 (8.4 per cent) were erroneously diagnosed as negative or benign conditions and subsequently proved to have a gastric malignancy. The breakdown of the false negatives is shown in Table VI.[1] It is fair to state that in 21 of the 72 false negatives, the diagnosis was equivocal. Although 91.6 per cent of patients with cancer of the stomach were definitely diagnosed by roentgenologic examination, in the 72 cases where the diagnosis was in error, 21 of these patients would have undoubtedly been explored for a more definite diagnosis.

The physician must employ all methods of diagnosis at his disposal and be aware that x-ray examination is not a means of diagnosis but an adjunct in our laboratory methods. He should not hesitate to request surgical exploration of the patient in whom cancer of the stomach is suspected, even though x-ray examination fails to demonstrate the lesion.

The burden of responsibility in diagnosing gastric cancer should not be heaped upon the roentgenologist entirely. An alert physician is still the "front line of defense" against this disease.

TABLE VI. INCIDENCE OF FALSE NEGATIVES BY ROENTGENOLOGIC EXAMINATION

		NO. CASES
1. The following diagnoses were advanced as being most likely:		46
Benign gastric ulcer	19	
Benign tumor	5	
Pyloric obstruction—benign	4	
Large gastric folds	4	
Deformity secondary to healed ulcer	3	
Extrinsic tumor	2	
Antral gastritis	2	
Cardiospasm	2	
Esophagitis with stricture	2	
Hiatus hernia	1	
Duodenal ulcer	1	
Incomplete (prepyloric ulcer correctly diagnosed)	1	
2. Roentgen examination considered negative		5
3. Roentgen examination equivocal.		
The differential diagnosis was between malignancy and conditions listed.		21
Pyloric obstruction—benign	11	
Benign tumor	2	
Antral gastritis	2	
Large gastric folds	1	
Benign gastric ulcer	1	
Bezoar	1	
Hypertrophic pyloric stenosis	1	
Negative	1	
Unsatisfactory examination	1	
	Total	72

Per cent false negatives (72/861)–8.4 per cent.

Operability, Resectability, and Lymph Node Involvement.—The operability, resectability, and lymph node involvement of the 1,152 patients seen between 1936 and 1949 is shown in Table VII. The operability rate was 73.6 per cent (848 cases) and resectability 49.9 per cent (575 cases) of all patients seen or 67.8 per cent of all patients who underwent operation. Exploratory laparotomy or palliative procedures other than palliative gastrectomy was performed in 23.7 per cent of all patients; partial gastrectomy in 492 patients (42.7 per cent) and total gastrectomy in 83 (7.2 per cent of all patients); 441 patients (38.3 per cent) underwent gastric resection with intent to cure.

The trend in operability and resectability from 1936 to 1949 demonstrates a 30 per cent increase in operability during the four-year period 1946 to 1949, as compared with a similar period ten years earlier. More than twice as many patients were considered resectable during the same later period in comparison with the early years; a 25 per cent increase in gastric resections is noted in operable cases during the same period. The percentage of "curative" resections had more than doubled during the ten-year interim. An increase in the percentage of "curative" resections of all patients operated upon was noted during the period 1940 to 1945, as compared with the previous four years. This remained constant during 1946 to 1949 despite the fact that an increase of 20

per cent of lymph node positive cases was noted during this period. Many of these patients would not have been afforded curative resections during the earlier years, 1936 to 1945. The increase in the number of patients with involvement of the regional lymph nodes suggests that an increasing number of late cases is being referred to this hospital for treatment. At the same time, however, the dissections of the lymph node-bearing areas in the region of the stomach has been extended. The analysis of lymph node involvement is limited only to those cases operated upon with intent to cure.

TABLE VII. A COMPARISON OF OPERABILITY, RESECTABILITY, AND LYMPH NODE INVOLVEMENT

	OPERABILITY		RESECTABILITY				
			ALL RESECTIONS		CURATIVE RESECTIONS		LYMPH NODE POSITIVE
YEARS	TOTAL NO. CASES	PER CENT	% ALL CASES	% CASES OPERATED	% ALL CASES	% CASES OPERATED	PER CENT
1936-39	241	57.3	27.8	48.6	22.4	39.1	50.0
1940-45	494	71.7	50.0	69.8	38.9	54.2	52.0
1946-49	417	85.4	62.6	73.3	46.8	54.8	70.3
1936-49	1152	73.6	49.9	67.8	38.3	52.0	60.1

In the fourteen-year period 1936 to 1949, 265 (60.1 per cent) of the 441 patients in which curative resections were performed had histologic evidence of lymph node involvement. A definite increase in the incidence of lymph node metastases has been noted from 1936 to 1949. During 1936 to 1939, 50 per cent of the cases had positive lymph nodes; 1940 to 1945, 52.0 per cent, and 1946 to 1949, 70.3 per cent. In the years 1947 and 1948, 75.0 per cent and 71.0 per cent, respectively, of the patients resected for cure had lymph node metastases. It is presumed that with the increase in the number of qualified, competent surgeons equally distributed in small communities and the larger number of well-equipped small community hospitals, gastric resection is not the formidable procedure of earlier years which was reserved only for the surgical staff of large University Centers. During the early years of this study only 3 to 4 surgeons performed all gastric resections for cancer at this hospital. Since 1950, the number of resections has been distributed among 12 surgeons. The University Hospitals, apparently, has been assuming more and more the role of a "court of final appeal" during recent years. The increased number of patients of advanced age as well as those with lymph node and distant metastases all tend to corroborate this assumption.

Hospital Mortality Rate.—The mortality rate for all operative procedures performed during the fourteen-year period was 13.7 per cent; explored, only 11.2 per cent; for all palliative procedures other than gastrectomy, 16.7 per cent; for all resections 13.7 per cent; partial gastrectomies, 12.6 per cent; and total gastrectomy 20.5 per cent. If we compare the trend in mortality rates for all operated cases, a marked improvement is noted. The mortality rates of all gastric resections including the total and partial resections performed during 1936 to 1939 was 38.8 per cent; 1940 to 1945, 12.1 per cent; and during the years 1946 to 1949, 8.8 per cent. The breakdown of the three periods into hos-

pital deaths of patients who were explored only, those who underwent palliative procedures other than resection, such as gastrostomy, enterostomy, and gastroenterostomy, and partial and total resections, is presented in graph form in Fig. 2. The mortality of the later period, 1946 to 1949, of 6.9 per cent for subtotal resections, is a marked decrease from that of ten years previously. During years 1945 to 1949, the hospital mortality rates following subtotal gastric resection for cancer rose above 10 per cent only in 1947. During 1945, 1946, 1948, and 1949, the mortality rates were 3.6, 3.9, 3.8, and 9.2 per cent, respectively. The hospital mortality of total gastrectomy during 1946 to 1949 was 14.8 per cent.

During 1949 only 1 patient (6.7 per cent) of the 15 in which total gastrectomy was performed for cancer of the stomach expired in the hospital. The most frequent cause of death following gastric resection for cancer of the stomach was peritonitis.

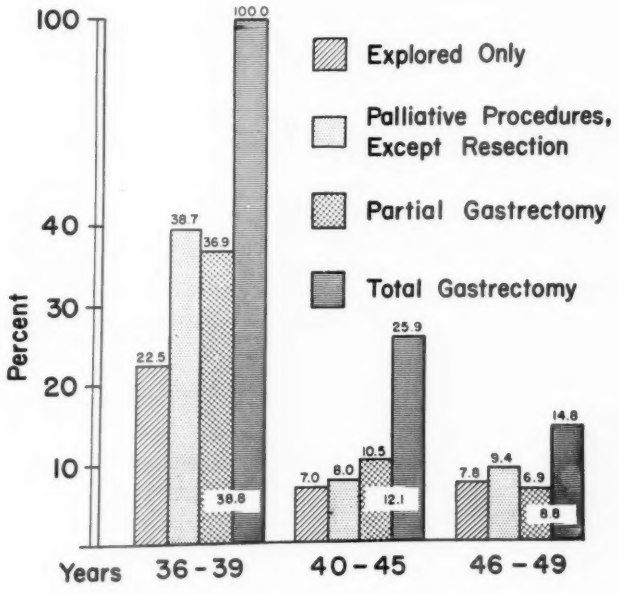

Fig. 2.—Mortality rate.

The inadvisability of gastrostomy, jejunostomy, and gastroenterostomy for obstructive nonresectable gastric cancer, as has been reported by Pack[22, 23] and others,[4, 15] is borne out when one compares Fig. 2 and Table VIII. Except for the period 1940 to 1945, the hospital mortality rate for patients who underwent palliative procedures other than gastrectomy was higher than in those patients who underwent palliative partial resection, or in the group that was explored only. Table VIII shows only little prolongation of life, as compared with those who were explored only, and a shorter period of survival than those who underwent palliative resections. It is our impression that a palliative resection should be performed whenever possible, as confirmed by the greater relief of symptoms it affords the patient in addition to the prolongation of life that has been noted with relatively low hospital mortality rate.

Five-Year Survival.—We previously stated that the presence or absence of lymph node involvement in gastric cancer patients has a much greater effect upon the five-year survival than the proficiency of the surgeon treating this disease. The five-year survival rates presented in our series bears this out. Of 441 patients who underwent gastric resection with the intention of cure, 60.1 per cent had evidence of lymphatic dissemination of the disease.

TABLE VIII. SURVIVAL TIME OF INCURABLE GASTRIC CANCER CASES

	MEDIAN SURVIVAL (MONTHS)	AVERAGE SURVIVAL (MONTHS)
No surgery	1	3.2
Explored only	3	4.4
All palliative procedures other than gastrectomy	4	5.0
Palliative partial gastrectomy	7	10.6
Curative gastrectomy	16	19.7
Palliative partial gastrectomy with hepatic metastases	5	6.7
Palliative procedures other than partial gastrectomy with liver metastases	3	4.5
Explored only and liver metastases found	2	2.8

The five-year survival rate for all cases seen at this hospital, including both outpatients and those admitted to the hospital for the entire fourteen-year period was 9.5 per cent (109 cases), and that of patients who underwent "curative resections," 24.7 per cent. The presence or absence of lymph node metastases had a fourfold greater effect upon survival than in those patients found to be lymph node negative. Forty-four per cent of lymph node negative cases survived five or more years after gastric resection, as compared with only 11.4 per cent of lymph node positive cases. Excluding operative mortality, the over-all five-year survival of patients in which curative gastric resections was employed was 28.6 per cent; of lymph node positive cases, 13.2 per cent; and lymph node negative cases, 51.6 per cent. In this same group, 55.2 per cent of lymph node negative cases and 16.9 per cent of lymph node positive cases who underwent "curative" partial gastric resection survived at least five years following operation. In the years 1948 and 1949, 72 per cent of lymph node negative curative resection survivors lived five or more years.

Only 2 of the 83 patients in which total gastrectomy was performed survived five or more years. One patient was lymph node positive and has been asymptomatic for the past seven years following gastric resection. The other patient is living and well at present, fourteen years after operation. A comparison of the three periods is presented graphically in Fig. 3. The percentage of positive and negative node five-year survivors is seen to have doubled in the ten-year interim with the over-all five-year survival having more than tripled during that same interval. This is a definite achievement, especially in view of the fact that 70.3 per cent of all cases resected for cure during the last four-year period had microscopic evidence of lymph node extension. Of the 109 patients who survived five or more years following gastrectomy for cancer of the stomach, 36 (33.0 per cent) survived over ten years (Table IX). Three patients survived longer than fifteen years, of which 2 are living and well.

TABLE IX. STATUS OF PATIENTS SURVIVING FIVE YEARS

	NO. + NODES	NO. − NODES	TOTAL
5-10 years	25	48	73
10-15 years	4	29	33
15-20 years	1	2	3

Carcinoma, 104; lymphosarcoma, 3; leiomyosarcoma, 2.

Extirpation of the Retropancreatic Nodes.—Innovations have been made since 1950 which may further improve these results. In the latter years of this study, it has been routine practice to excise the spleen and splenic pedicle along with the omentum in every case of gastric cancer, in order to remove a large area of gastric lymph node drainage. At present, in addition to the aforementioned, the distal pancreas is removed if gross involvement of nodes along the superior border of the pancreas is noted or if there is direct extension into this area. There is increased stress on performing lymph node dissections in the region of the cardia and porta hepatis to the portal triad. The dissection is continued by resecting the tail of the pancreas, anteriorly, to include the retropancreatic nodes.

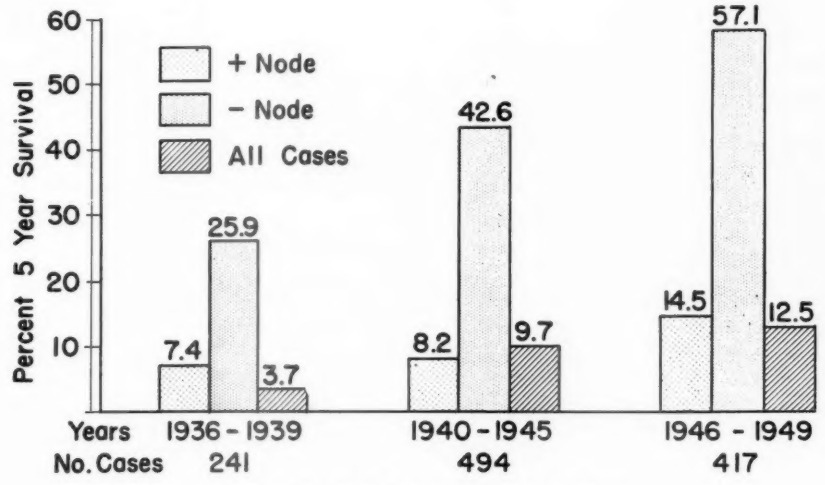

Fig. 3.—Trend in five-year survival.

Extirpation of the retro- and periduodenal nodes[2] is accomplished by continuing the dissection along the common duct and portal vein. Wangensteen[31] first advocated and performed these dissections in 1948, but this wide extirpation did not become routine practice at this hospital until 1952. The use of midline upper abdominal incisions in conjunction with sternotomy offers excellent access to the cardia and lower esophagus, enabling the surgeon to perform a much more thorough dissection in this area.

Fig. 4 demonstrates in graphic form the trend in operability, resectability, mortality, and five-year survival for each year. A continuous improvement in hospital mortality rate and five-year survival rates is evident.

Curative resections were performed in 38.3 per cent of all cases seen and 73.6 per cent of all patients operated upon. What was attempted and what was

accomplished in the 35 per cent of cases which lay between is presented in Table VIII. Since 1944, no patient who was considered inoperable has survived longer than seven months. The average survival rate of this group after surgical consultation was 3.2 months; fifty per cent of patients in this series expired within one month. In a slightly better group of cases, exploration only was carried out. The average duration of survival was 4.4 months and 50 per cent were dead within three months after operation.

In a third group of patients, the disease was too far advanced to warrant a palliative resection in the judgment of the surgeon. In this group, gastrostomy, enterostomy, or gastroenterostomy was performed for nutritive purposes or where signs of impending obstruction was evident. The average length of survival was five months; fifty per cent were dead within four months. The efficacy of this treatment as compared with those patients who were explored only is not significantly better. When one reviews the hospital mortality rate of this group of patients, which was significantly greater than in the group that underwent exploration only, the advisability of these palliative procedures is

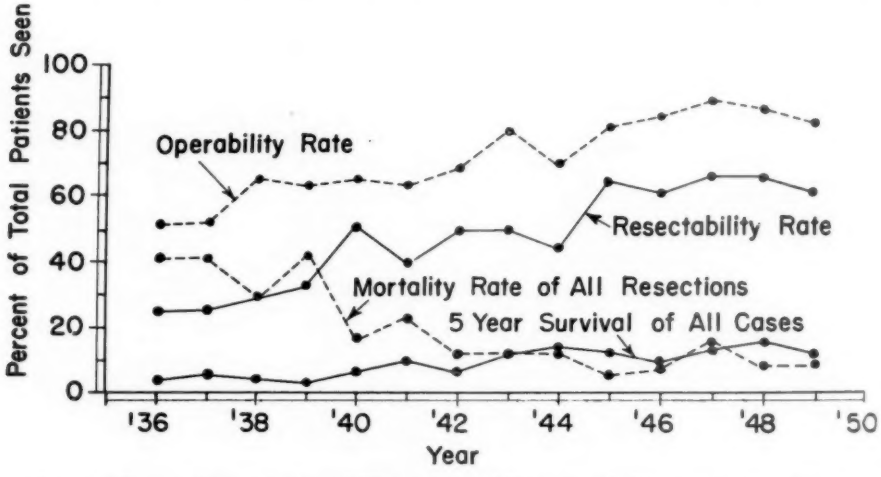

Fig. 4.—Comparison of operability, resectability, mortality, and five-year survival.

questioned. In contradistinction, the rationale of palliative partial gastric resection for incurable cases is enhanced by the fact that the average duration of life was 10.6 months, one-half living at least seven months following resection. The hospital mortality of this group was no greater than that noted in the patients who underwent other types of palliative procedures.

An attempt has been made to select from this group of cases subgroups which might aid in determining the benefit derived from palliative gastric resection in the presence of liver metastases. No patient with liver metastases survived five years following gastrectomy. It must be stressed that by liver metastases we do not mean direct extension of the primary tumor into the adjacent liver by adherence of the neoplasm from the stomach to the liver, for two such cases are among the five-year survivals. The term "liver metastases" is interpreted as lymphatic extension to the liver. Resection of the stomach in the presence of liver metastases afforded two to four months' prolongation of life

as compared with the performance of palliative procedures or exploration alone in their presence. The relief of pain associated with the prevention of early cancerous obstruction that this procedure affords a majority of patients validates its employment whenever possible, in the judgment of the surgeon.

An analysis of five-year losses for comparison during the periods 1936 to 1939 and 1946 to 1949 is presented in Fig. 5. The salvage of 9 additional patients per 100 patients seen at this hospital in 1949 can be interpreted as a direct result of the increased stress for attempts at curative resections during that period. The fact that, in spite of the number of lymph node positive cases having increased approximately 20 per cent during that period, a marked improvement in five-year survival occurred, only enhances the advisability of performing more extensive lymph node dissections.

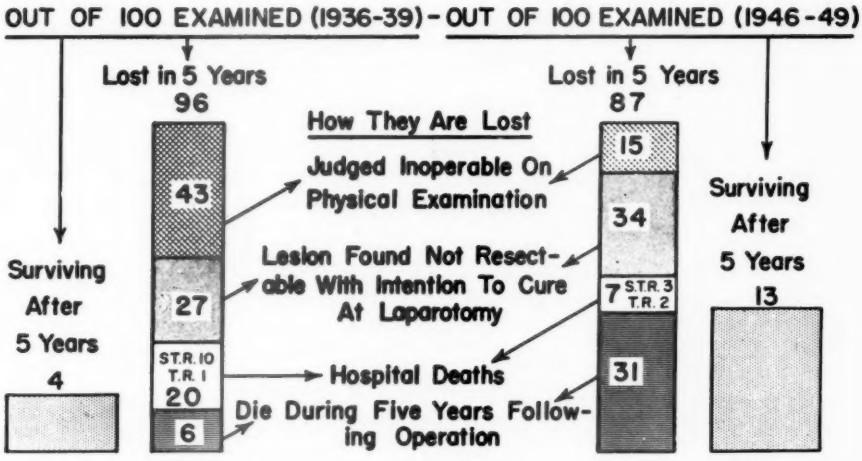

Fig. 5.—Analysis of five-year losses.

DISCUSSION

Carcinoma of the stomach has been considered the most frequent type of cancer to cause death. In 1948, there were over 26,000 deaths due to gastric cancer in the United States.[30] In 1953, 53.7 deaths per 100,000 population were the result of gastric cancer, as compared with 17.9 per 100,000 in 1948.[28] In spite of intensive efforts by various cancer groups to enlighten the layman and the physician as to the early signs and symptoms of this disease, no significant shortening in the delay from the onset of symptoms to surgical therapy has been noted. Patients are not presenting themselves to their physicians any earlier and physicians are not referring patients with gastric cancer to the surgeons any sooner. The common complaint of "indigestion" in middle or late life should be thoroughly investigated. A simple means of screening can be performed by any physician in his office. This includes hemoglobin determination, aspiration of gastric contents for free hydrochloric acid, and examination of the feces for occult blood. Should any of these tests vary from the normal, or

TABLE X. OPERABILITY, RESECTABILITY, AND SURVIVAL; REPORTS OF VARIOUS AUTHORS

AUTHOR	YEARS	NO. OF CASES	OPERABILITY (PER CENT)	RESECTABILITY (PER CENT)	PER CENT RESECTION MORTALITY	PER CENT LYMPH NODE POS. CASES	5-YEAR SURVIVAL			
							PER CENT RESECTION SURVIVORS	PER CENT LYMPH NODE POS.	PER CENT LYMPH NODE NEG.	PER CENT TOTAL CASES
Berkson et al.[3] (Mayo Clinic)	1940-49		80.0	44.0	8.0	1907-49 58.9	34.8	18.6	48.5	14.0
Brown and Kane[6] (Cleveland Clinic)	1940-45	406	68.0	25.0	9.0					7.1
Guiss[13] (Los Angeles Hosp.)	1930-39	1,295	38.6	7.7	46.0		1930-49			1930-49*
	1940-49	1,596	41.0	12.8	21.2		33.6			1.4
Jemerin and Colp[15] (Mt. Sinai, N. Y. Hosp.)	1938-42	157	93.6	41.0	35.0		23.8			6.4*
	1943-47	187	99.0	52.0	20.0		27.3			11.6*
Lawton et al.[17] (Univ. of Illinois)	1931-47	1,004	62.8	31.9	17.0					4.7†
Maimon and Palmer[18] (Billings, Chicago)	1927-44	466	83.5	43.5	Before 1940 22.6 After 1940 16.3		32.2			
Ochsner et al.[20] (Tulane)	1942-54		80.3	37.0				12.0‡	57.6‡	7.2‡
Pack and McNeer[22] (Memorial Hosp.)	1937-41	278	73.7	26.2	19.2	1916-41			1916-41	
	1942-46	405	82.7	39.8	21.7	30.8	34.7	24.2	42.8	3.4
Ransom[24] (Univ. of Michigan)	1934-40	609	55.0	35.9	21.5	1934-46	31.5		1934-46	8.2
	1941-46	655	64.4	36.3	15.1	70.0	25.0	15.8	49.5	7.0
Welch and Allen[32] (Mass. Gen. Hosp.)	1937-41	375	75.0	46.0	26.0					
	1942-46	457	77.0	53.0	11.0					7*
Wilson[33] (Stanford U.)	1929-38	108	57.0	25.0	37.0				1919-43	
	1939-48	120	85.0	42.0	6.0		23.0			4.6
This series	1936-39	241	57.3	27.8	38.8	50.0	26.5	7.4	25.9	3.7
	1940-45	494	71.7	50.0	12.1	52.0	28.6	8.2	42.6	9.7 9.5§
	1946-49	417	85.4	62.6	8.8	70.3	29.0	14.5	57.1	12.5

*Only admissions to hospital.
†Only male hospital admissions.
‡Subtotal resections only.
§From 1936-1949 all cases including outpatient and inpatient.

should symptoms persist, then roentgenologic examination of the stomach should be performed and repeated at short intervals if early examinations are inconclusive.

It has been reported that twenty months elapse from the onset of the disease until symptoms present themselves. If an additional six months (median delay) are added during which the delay from onset to treatment occurs, a total of twenty-six months has elapsed before treatment is afforded. It is therefore evident that with our present means of diagnosis, little can be expected in improving the five-year survival by so-called "early detection." The burden of responsibility therefore rests with the surgeon in attempting to salvage as many patients as possible. The improvement in results of therapy for cancer of the stomach can only be achieved by affording every patient an opportunity for cure. This entails exploration with intention of performing a curative resection whenever possible. The term "curative resection" encompasses extirpation of the stomach, well beyond the confines of the primary lesion, in addition to the wide excision of all known lymph-bearing areas. Resection of adjacent organs which are involved by direct extension should be performed as well. The innovation of "second-look" operations has definitely demonstrated routes of spread which were hitherto unknown. This information should enable surgeons to extend the operation for gastric cancer to include excision of the entire potential regional areas of lymphatic spread.

The increase in over-all five-year survival since 1936 is to be considered a direct result of the surgeon's ever-increasing aggressiveness in approaching this problem. It is too early to evaluate the results of our present policy of treatment of gastric cancer as described here, but it is believed that some further improvement in survival will be noted.

Although it is not the purpose of this paper to compare results of therapy, the increase in the percentage of five-year survivors following gastric resection for cancer of the stomach has been noted by other investigators, as shown in Table X.

SUMMARY

1. The University of Minnesota Hospitals' total experience with gastric cancer from 1936 to 1949 is presented. Eleven hundred and fifty-two cases of cancer of the stomach were seen at this hospital from 1936 to 1949. Eighty-one per cent had histologic or operative evidence of gastric cancer.

2. The delay from onset of symptoms to surgical treatment has not been shortened significantly during this period.

3. During the years 1936 to 1949 the average age of all patients was 62.8 years. A steady increase in older age patients has been noted. Three times as many men as women had gastric cancer.

4. Examination of aspirated gastric contents for free hydrochloric acid and stool examination for occult blood are two important tests which may assist in the early detection of gastric cancer. Achlorhydria and/or hypochlorhydria was noted in 87.8 per cent of all patients tested; 83.2 per cent of all patients in

which occult blood in stools were examined by guaiac test were found to be positive. These are two simple tests which can be performed in the physician's office.

5. A steady increase in operability and resectability is noted with a resection mortality of 8.8 per cent during 1946 to 1949.

6. Five-year survival rates have increased from an over-all rate of 3.7 per cent during 1936 to 1939 to 12.5 per cent during the period 1946 to 1949. The five-year survival rate during the entire fourteen-year period of patients undergoing resection for cure who were subsequently found to have lymph node involvement with tumor was 11.4 per cent; of those found to be lymph node negative, 44.1 per cent survived five or more years. During 1946 to 1949, over 70 per cent of patients resected for "cure" were lymph node positive, of which 14.5 per cent survived five years or more. During this same period, 57.1 per cent of lymph node negative cases survived five years after gastric resection was performed.

7. The role of the surgeon is continually increasing in importance for improving the five-year cure. Knowledge gained through "second-look" operations should enable us to continue to improve the five-year survival rate in the future.

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GASTRODUODENAL ULCERATION COMPLICATING OTHER DISEASES

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WE HAVE been distressed by the frequency with which gastroduodenal ulceration has occurred as a complication in our patients (Fig. 1). Roessle[13] recognized this complication and, in 1913, he referred to it as "die Zweite Krankheit." In this paper we shall present 31 instances of secondary gastroduodenal ulceration. Brief references will be made to theoretical aspects of this problem.

CASE REPORTS

We have included in our series only those cases which gave no history of ulcer prior to the onset of the main disease process. We have included not only superficial erosions but also ulcers which have bled massively or perforated. In many instances, death was caused by the complicating ulcer rather than by the primary disease process. No attempt has been made to separate a special type of acute stress ulcer. Twenty-eight of these cases were collected from 566 consecutive autopsies at the Seattle Veterans Administration Hospital from April, 1951, to July, 1954. In one case the diagnosis was made at laparotomy. Two additional cases were kindly permitted us.†

CASE 1.—Multiple sclerosis was diagnosed in 1947, and Hodgkin's disease was diagnosed in 1950 in this 32-year-old white man. The patient had been treated with nitrogen mustard and x-ray therapy. At the time of admission to this hospital he weighed 80 pounds. There was pitting edema and decubitus ulceration. At autopsy, Dec. 17, 1951, the mucosal lining of the first portion of the duodenum was notably hyperemic and on the anterior aspect of the first portion of the duodenum there was an acute hemorrhagic ulcer, 1.5 mm. in diameter. The ulcer was punched out with a soft, nonelevated margin. Black tarry material resembling old blood was seen in abundance throughout the remaining small and large bowel, all of which was lined with intact mucous membrane.

CASE 2.—This 55-year-old white man had a right colectomy for carcinoma in 1936. He had a prostatectomy in 1950 for benign disease, and in 1950 the remaining colon was removed for malignancy. The patient had multiple metastases and his weight had declined from 160 pounds to 132 pounds. He vomited blood the day before his death. At autopsy on Aug. 12, 1951, there were many metastatic nodules in the liver. The stomach showed several mucosal erosions 12 to 18 mm. in diameter. In the center of one fundal erosion there was a small blood vessel. The duodenum contained two shallow mucosal ulcers, 1.8 cm. and 1.9 cm. in diameter. These ulcers had sharp borders and were somewhat deeper than their counterpart seen in the stomach. The remainder of the small bowel was filled with bloody fluid throughout its entire length.

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†One by Dr. Robert P. Glover[7] and one by Dr. E. J. Strode.[18]

CASE 3.—This 61-year-old white man had a rectal carcinoma with a rectal fistula. At autopsy on Aug. 3, 1951, there was a large, deep, punched-out ulcer crater, approximately 3.5 cm. in diameter, adjacent to the pyloric ring. This ulcer had penetrated into the liver parenchyma and it also communicated with subdiaphragmatic abscess. The small bowel and the large bowel were filled with black tarry material which looked like old blood. There were bilateral adrenal metastases.

CASE 4.—This 59-year-old white man received shock therapy for psychoneurosis. His weight had diminished from 165 pounds to 100 pounds in the past two and one-half months. The peritoneal cavity at autopsy, on July 20, 1951, contained 4,000 c.c. of cloudy, bile-stained fluid and had fibropurulent adhesions. The gastric mucosa had three small areas punched out by superficial erosions and multiple areas of submucosal hyperemia. A 1.5 cm. perforation occurred in the first portion of the duodenum.

CASE 5.—This 38-year-old white man had a carcinoma of the lung and his weight had diminished from 133 to 119 pounds. At autopsy on May 2, 1953, the stomach and esophagus contained approximately 500 c.c. of black bloody fluid. In the stomach there were numerous superficial ulcers measuring from 12 to 13 mm. in diameter. These had hemorrhagic bases and were scattered throughout the fundus and along the greater curvature.

CASE 6.—This 38-year-old white man had pleural effusion for four months. At autopsy on April 21, 1953, there was extensive carcinomatosis with no definite primary tumor. There was a rounded, indurated, prepyloric ulcer, 1.0 cm. in diameter and 0.4 cm. deep. On the pyloric ring, there was a 0.5 cm. ulcer. Two centimeters distal to the pylorus on the posterior wall there was another large ulceration, approximately 2 cm. in diameter.

CASE 7.—This 37-year-old white man had a diaphragmatic hiatus hernia, with transthoracic repair on Nov. 10, 1952. The subsequent course included paraplegia and marked depression. He had a massive hematemesis and, at surgery on May 13, 1953, a severely bleeding superficial cardioesophageal ulcer was fulgurated with cessation of bleeding, but the patient's condition deteriorated and he expired May 20. No autopsy was permitted.

CASE 8.—This 58-year-old white man had peripheral arteriosclerosis for which he received lumbar sympathetic blocks. On July 18, 1951, the patient went into shock and expired. At autopsy on this date the peritoneal cavity contained air and 2,500 c.c. of foul-smelling gray fluid with generalized distribution of purulent exudate. On the superior surface of the pylorus, just proximal to the pyloric ring, there was an irregular ragged perforation from which some of the contents exuded. There was an oval, sharply punched-out ulcer on the pyloric antrum measuring 3 cm. by 1.5 cm. The edges were sharp and the base was ragged and necrotic.

CASE 9.—This 40-year-old white man had carcinoma of the right lung with metastases. At autopsy on Aug. 10, 1952, there was a 1 cm. perforated duodenal ulcer with minimal inflammatory reaction adjacent to the ulcer.

CASE 10.—This 56-year-old white man had cirrhosis with primary hepatic carcinoma. He had received cortisone therapy in small amounts. At autopsy on May 11, 1953, there were large esophageal varices. The entire gastrointestinal tract was filled with blood. The duodenum contained two large ulcers with erosion of the pancreaticoduodenal artery.

CASE 11.—This 45-year-old white man had a right pneumonectomy in January, 1952, for carcinoma of the lung. He subsequently developed superior vena caval obstruction. At autopsy on June 10, 1952, the stomach was filled with what appeared to be old blood. There was a fresh ulcer on the pyloric ring measuring 1.0 cm. in diameter. The base was filled with what appeared to be clotted fresh blood.

CASE 12.—This 52-year-old man had myocardial infarction which had been treated during the previous thirty-six hours with Levophed. At autopsy on Nov. 25, 1952, the duodenum contained bloody fluid and was hyperemic. Three centimeters distal to the pyloric ring there was a shallow healed ulcer, 1.5 cm. in diameter. About 3 cm. distal to this lesion there was another ulcer about the same size.

CASE 13.—This 82-year-old man had carcinoma of the rectosigmoid with metastases to the abdominal wall and malnutrition. For eight weeks prior to death, a Miller-Abbott tube had been incarcerated in the upper intestinal tract. At autopsy on April 29, 1953, there was an ulcer at the cardiesophageal junction, 1.0 cm. in diameter. On the lesser curvature there was an ulcer 2 cm. by 3 cm. which extended into the musculature of the stomach.

CASE 14.—This 56-year-old white man had a carcinoma at the head of the pancreas. During the course of his illness he developed a perforating gastric ulcer which was successfully closed. He was markedly cachectic. His treatment had included 30 c.c. of whiskey during the last several days of life and he had had gastrointestinal bleeding during this period of time. At autopsy Aug. 28, 1952, the stomach contained 300 c.c. of bloody material. There was a shallow duodenal ulcer 18 mm. in diameter on the anterior wall. The ulcer overlay a metastatic tumor. There was a black tarry material partially filling the lumen throughout the entire small bowel and ascending and transverse colon.

CASE 15.—This 51-year-old white man developed a bronchopleural fistula and empyema three years after a right pneumonectomy. At autopsy on Jan. 31, 1953, there was a superficial gastric ulcer in the mid-portion of the lesser curvature measuring 1.0 cm. by 0.5 cm.

CASE 16.—This 65-year-old white man had an inoperable carcinoma of the right lung with superior vena caval obstruction. Twenty-four hours before death he passed bloody stools. An autopsy on Feb. 6, 1954, showed an acute duodenal perforation with peritonitis.

CASE 17.—This 37-year-old Alaskan Eskimo had marked aortic insufficiency. Autopsy on March 2, 1954, showed a syphilitic aortitis. On the lesser curvature near the pylorus, were two acute ulcers, measuring 0.3 cm. and 0.5 cm. in diameter.

CASE 18.—This 70-year-old man had sharp pains in the arms, legs, and trunk of 4 months' duration. He had had fecal and urinary incontinence for one week. There were marked weakness and atrophy of both legs. He was treated with codeine and cortisone. He suddenly lapsed into coma and expired on May 16, 1954. Autopsy on that date revealed pleomorphic and undifferentiated bronchogenic carcinoma with metastases to the skull, vertebra, and pleura. Distal to the pylorus was an acute duodenal ulcer measuring 1.0 cm. by 1.5 cm. which had penetrated the muscularis.

CASE 19.—This 33-year-old man had carcinoma of the liver with jaundice for about seventeen months. During the course of the patient's illness a duodenal ulcer was discovered in the medical work-up of this patient. At autopsy on Feb. 9, 1954, there was a punched-out duodenal ulcer penetrating the duodenal wall and there was a tumor in the base of the ulcer which was apparently contiguous with the carcinoma of the liver.

CASE 20.—This 43-year-old white man gave a history of cerebral vascular accident presumably due to a ruptured aneurysm. At autopsy June 14, 1954, there was a ruptured aneurysm of the circle of Willis. Near the cardioesophageal junction there was an ulcer communicating with an abscess cavity in the subdiaphragmatic space.

CASE 21.—This 65-year-old white man had carcinoma of the prostate with multiple metastases. During his terminal illness he required medication for relief of abdominal distress. On Aug. 23, 1954, the patient became very pale and expired. Autopsy on this date revealed that the stomach contained about 1,500 c.c. of dark-red, clotted blood. Distal to the pylorus on the posterior wall was a round ulcer approximately 4.0 cm. in diameter which penetrated into the head of the pancreas and which was filled with fresh blood clots.

CASE 22.—This patient gave a history of lupus erythematosus and bacterial endocarditis. At autopsy on Nov. 25, 1953, on the posterior wall of the duodenum approximately 1 cm. beyond the pyloric valve there was a large circular penetrating ulcer which measured 3 cm. in its largest diameter. The edges of the ulcer were not indurated or scarred (Fig. 1).

CASE 23.—This 50-year-old Filipino had cirrhosis and portal hypertension for which a portacaval shunt had been performed on Jan. 29, 1952. The autopsy on Feb. 21 showed cirrhosis with esophageal varices and the portacaval shunt was patent. The duodenum contained an ulcer crater approximately 1.5 cm. and 3.0 in area and 1.0 cm. deep on the superior aspect of the first portion of the duodenum.

CASE 24.—This 64-year-old white man had a carcinoma of the lung with extensive metastases. At autopsy on March 3, 1954, the peritoneal cavity contained feculent, gaseous material and fluid. There was a 4 cm. circular ulcer which was probably primarily present in the duodenum but had trespassed the pylorus and had infringed upon the stomach mucosa. The ulcer had perforated through the greater and lesser sac.

CASE 25.—This 58-year-old patient had Hodgkin's disease. He received cortisone terminally. At autopsy on May 3, 1954, the stomach contained a moderate amount of liquid and black fluid. Scattered along the greater and lesser curvature there were areas of acute antemortem ulceration. Two large ulcers were located along the greater curvature and the larger of these measured 2.5 cm. in diameter. In addition to the two ulcers noted along the greater curvature, there were two smaller ulcers on the lesser curvature.

Fig. 1.—Gross specimen from Case 22 showing a large duodenal ulcer. This patient had lupus erythematosus and bacterial endocarditis.

CASE 26.—This patient, aged 65, had a carcinoma of the lung. At autopsy on March 16, 1954, there was a sharply demarcated area of ulceration 2 cm. distal to the pyloric ring on the posterior surface of the duodenum.

CASE 27.—This 65-year-old white man had a carcinoma of the lung with metastases. He had been treated with x-ray therapy. At autopsy on June 26, 1954, in the prepyloric area there were approximately six ulcerations of the mucosa varying in size from 4 cm. to 1.2 cm. in diameter. The smaller ones appeared to be very superficial.

CASE 28.—This white man, aged 66, had been treated for glioblastoma multiforme. In the latter days of his illness he had tarry stool with coffee-ground-like emesis. At autopsy on July 21, 1953, there was a small ulceration of the mucosa approximately 0.3 cm. in diameter overlying the pylorus.

CASE 29—This patient was cared for by Dr. Robert P. Glover[7] who reported that the patient had developed an acute prepyloric ulcer after the excision of a ventricular aneurysm. The ulcer may have been related to the source of this patient's fatal hemorrhage.

CASE 30.—Information on this patient was kindly supplied to us by Dr. E. J. Strode.[18] The patient developed a carcinomatosis from a breast cancer. Following bilateral adrenalectomy and subsequent cortisone therapy, she developed an acute ulcer. Dr. Strode felt that in this patient's case cortisone was probably an exciting factor in producing the ulcer.

CASE 31.—This 22-year-old clerk had abdominal pain in the fall of 1953; in March, 1954, he had left lower quadrant ache and cramps in both legs after exercise. Lymph node biopsy suggested polyarteritis. Cortisone therapy was given. The sputum was positive for acid-fast bacilli. Except for positive guaiac stools he had no evidence for ulcers. At necropsy there were perforated duodenal and esophageal ulcers.

SUMMARY OF THE SERIOUS CONSEQUENCES OF SECONDARY GASTRODUODENAL ULCERATION

HEMORRHAGE	PERFORATION	POSSIBLY RELATED TO DEATH
10	8	15

DISCUSSION

A review of the literature on the subject of what might be called secondary gastroduodenal ulceration reveals a multiplicity of terms. To name a few examples, there are Curling's[1, 8] ulcer, Cushing's[2] ulcer, stress ulcer,[15] hunger ulcer,[16] air-raid ulcer,[16] and postoperative ulcer.[10] Fletcher and Harkins[4] emphasized that gastroduodenal ulceration occurs after a variety of antecedent stresses, whereas originally it had been thought that extensive burns were the chief, if not the only, exciting mechanism.

The statistical difficulties in evaluating this problem were emphasized by Harkins[8] in his study of Curling's ulcer. The statistical incidence of peptic ulceration accompanying other diseases at necropsy was studied by Mears,[11] who reviewed one thousand consecutive autopsies. Excluding cases in which peptic ulceration had caused death primarily by perforation or hemorrhage, Mears found that there were 32 cases in which gastric or duodenal erosions or ulcer were present as a finding associated with other primary pathologic lesions causing death, an incidence of 3.2 per cent. Fletcher and Harkins[4] found an incidence of 1.2 per cent acute gastroduodenal ulceration in a series of 4,102 autopsies at King County Hospital. We reviewed 566 consecutive autopsies from April, 1951, to July, 1954, at the Seattle Veterans Administration Hospital. In our autopsy series there were 28 (4.9 per cent) instances of gastric or duodenal ulceration secondary to other disease processes. We included ulcerations which resulted in fatal hemorrhages or perforations. No attempt was made to distinguish a specific type of stress ulcer, and our series was not limited to acute ulcers.

Hunter's[12] remarks about the function of the stomach are interesting to recall.* However, since his day much valuable information has been obtained relative to the role of the stomach and the mechanism of gastroduodenal ulcer formation. Dragstedt[3] commented:

> That a hypersecretion of gastric juice may be the primary cause of duodenal ulcer is indicated by the fact that a hypersecretion of similar degree in experi-

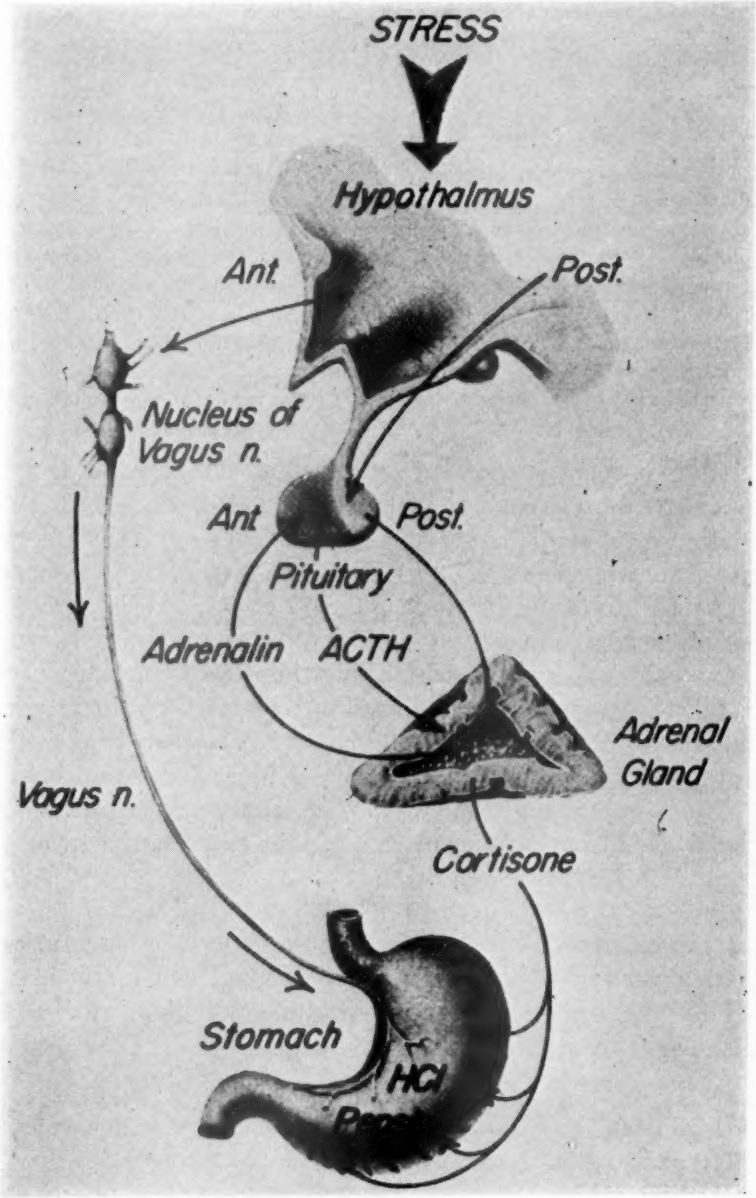

Fig. 2.—Schematic outline of the interrelationship suggested by Shay[17] to explain ulcer pathogenesis. (From Shay, Gastroenterology, 1954.)

*"Some physiologists will have it that the stomach is a mill; others that it is a fermenting vat; others again, that it is a stew pan, but in my view of the matter, it is neither a mill, a fermenting vat, nor a stew pan—but a stomach, gentlemen, a stomach."

> mental animals regularly leads to peptic ulcer formation and the abolition of this hypersecretion by complete gastric vagotomy in man causes the duodenal ulcer to heal. It remains to be demonstrated, however, that the tensions and strains encountered in the daily life of duodenal-ulcer patients provide adequate stimulation for the hypothalamic pituitary axis. However, the occurrence of peptic ulceration after severe burns, perhaps as Curling's ulcer, and other serious trauma could be dependent upon this mechanism since there is better evidence that these severe bodily stresses excite the adrenal mechanism. Further investigation in this field will be awaited with great interest.

Shay[17] discussed the pathogenesis of peptic ulcer and represented his concept in Fig. 2.

French and associates[5] noted that:

> During experimental stress (anoxia, hypoglycemia, infection or epinephrine) a tremendous augmentation of spontaneous electrical discharge can be recorded from this same portion of the hypothalamous (posterior). Delayed secretion of hydrochloric acid by the stomach as mediated by the pituitary-adrenal system may be considered a manifestation of stress. As such, the expression of its influence on the gastro-intestinal tract would be abnormal as distinct from those conducted by way of the vagus nerve which presumably are exerted daily in the normal process of alimentation—both vagal and humoral influences emanate from hypothalamic areas readily available to the rigors of emotional turmoil by virtue of their known rich connections with other cerebral structures (Fig. 2).

Lillehei and co-workers,[9] however, directed attention to the fact that a number of stress provoking agencies in experimental animals failed to influence gastric secretion or even depress gastric acidity, but nevertheless, they exerted powerful ulcer abetting effect by reducing the resistance of the gastroduodenal mucosa to gastric digestion.'' It is possible that there is a relationship between gastrointestinal congestion and hemoconcentration, as suggested by Friesen.[6] A recent observation which may implicate the adrenal mechanism, however, is the observation by Sandberg and associates[14] that dying is invariably associated with a high level of plasma 17-hydroxycorticoids. It is evident that our knowledge of the intimate details of ulcer formation is at present incomplete. There is evidence, however, that whatever the specific mechanism, gastroduodenal ulceration does occur as a serious complication of other diseases.

SUMMARY

We have presented 31 instances of gastroduodenal ulceration occurring secondary to a variety of other disease processes. In many instances death was caused by the secondary gastric or duodenal ulcer rather than by the primary disease.

CONCLUSIONS

1. We feel that the classification of these ulcers under various headings only serves to obscure the basic problem of ulcer pathogenesis.

2. Until this serious complication can be prevented, we must be alert to suspect its onset in patients who already may present various diagnostic and therapeutic problems.

We wish to express our appreciation to Prof. Henry N. Harkins for advice and encouragement in the preparation of this paper.

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FURTHER APPLICATION OF THE ENTEROHEPATIC CIRCULATION OF BILE ACIDS TO A STUDY OF THE PATENCY OF A PORTACAVAL SHUNT

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THE treatment of portal hypertension by a shunt between a vein of the portal system and a systemic vein is now an accepted procedure. The optimal clinical indication for such an operation appears to be a history of bleeding esophageal varices in the absence of ascites and jaundice. The results, as judged by the prevention of further exsanguinating hemorrhage, are good.

The type of shunt employed depends partly upon the etiology of the portal hypertension in that extrahepatic portal bed block necessitates a splenorenal anastomosis, whereas intrahepatic portal bed block provides an opportunity for a portacaval anastomosis as well as a splenorenal anastomosis. The relatively greater diameter of the portal vein as compared with the splenic vein makes the probability of continued patency of a portacaval shunt reasonably greater than that for a splenorenal shunt, especially when the former is the end of the portal vein into the side of the inferior vena cava. Granted that a portacaval anastomosis has the better chance to remain patent, one then has a choice between a side-to-side or an end-to-side type of anastomosis.

Observations on dogs have been made which suggest that a side-to-side portacaval anastomosis, in which the liver is not deprived of all the portal vein inflow, will result in less liver dysfunction than that which occurs following complete portal blood diversion, as must occur in an end-to-side shunt. There is a relatively greater impairment of Bromsulphalein excretion in dogs by the liver following an end-to-side shunt as compared with no impairment following a side-to-side shunt.[7] Furthermore, the choleretic effect of duodenally administered bile salts in calling forth a vigorous flow of hepatic bile persists after a side-to-side shunt in dogs but is markedly impaired following an end-to-side shunt.[1, 2]

Despite these observations, the efficacy of a side-to-side shunt may be questioned on the basis that over a period of time the shunt can be expected to close, since neither of the efferent limbs is obstructed. Accordingly, a test of the patency of a shunt has been devised in dogs using the enterohepatic circulation of bile acids. This test is based upon the ability of the liver in the

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absence of a shunt to keep the level of peripheral bile salt at a constant level, despite any variation in intestinal absorption of the bile salt. A patent shunt necessarily by-passes the liver, thereby resulting in elevations of peripheral bile salt.

As previously reported following the construction of a portacaval shunt of either type in dogs, bile salt was administered duodenally in the amount of 100 to 200 mg. per kilogram of body weight. Within two hours a maximum elevation of peripheral bile salt in the magnitude of about five to ten times the normal was demonstrable, thereby indicating a shunt to be patent. Closure of a shunt, as demonstrated at necropsy, was followed by no rise in peripheral bile salt after the administration of a like amount of bile salt duodenally. Similarly, in the control experiments in which an animal was tested without the presence of a shunt, there was no rise in peripheral bile salt. The conclusion was reached that an elevation of peripheral bile acids after the introduction of enteral bile salt in a shunted experimental animal could be interpreted as indicating that the shunt was patent.[1, 2]

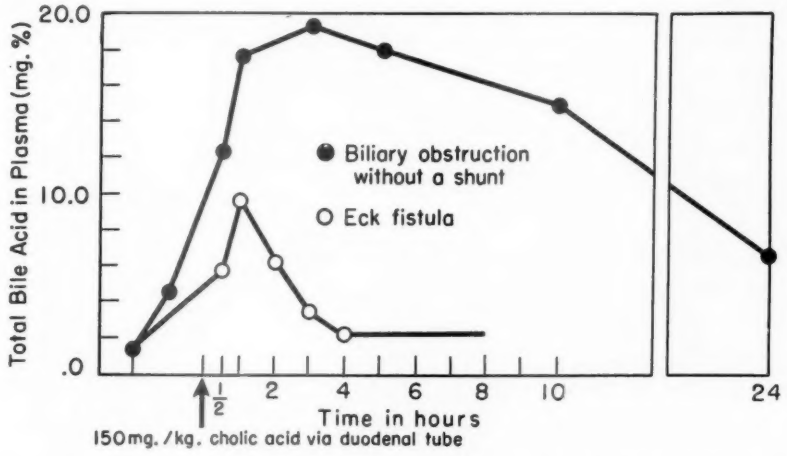

Fig. 1.—Total bile acid in peripheral blood after (1) duodenal administration of cholic acid in biliary obstruction, and after (2) Eck fistula. Average of 6 experiments.

The Effect of Exogenous Bile Acid Administration in the Presence of Acute Bile Duct Obstruction.—Further experiments, which we will not report, have demonstrated that in certain other situations there will be a rise in peripheral bile acids following their administration duodenally. This may occur in the absence of a shunt and appears to accompany acute obstruction of the common bile duct. The two situations, however, can be differentiated by an examination of the character of the curve representing the peripheral total bile acid concentration plotted against the time interval following the duodenal administration of bile salt.

Experiments.—Four medium-sized dogs were prepared by ligation of the common bile duct followed by a cholecystectomy. A portacaval shunt was not performed. Postoperatively, the bile duct obstruction was allowed to exist for from one to three days, after which the bile acid circulation studies were

made. Total bile acids were determined by a photofluorometric method which was developed in this laboratory.[1, 3] Fig. 1 shows the average of six such experiments as compared with the original experiments with an Eck fistula. As in the shunted animals, there occurred an increase in the peripheral total bile acids following the administration of cholic acid into the duodenum. However, there are significant differences in the levels of peripheral bile acids which make it possible to differentiate a patent shunt from an acutely obstructed biliary duct. In the latter cases the maximum elevation is appreciably higher and persists over a much longer time interval. A measurable increase in peripheral total bile acid concentration was observed at intervals, starting from thirty minutes and up to ten hours after duodenal administration of cholic acid. The highest concentration occurred in from three to five hours and subsequently the concentration fell slowly over a period of twenty-four hours or more.

These curves are contrasted with those previously reported as accompanying a patent shunt. In such cases, there is a maximum elevation of peripheral total bile acids of about five to ten times the normal. Furthermore, this maximum elevation occurred within two hours after the enteric introduction of bile salts and was followed by a rather rapid fall. There was no elevation of peripheral bile acid after the four-hour period. It would seem, therefore, that the experiments involving a patent shunt can be differentiated from those involving acute bile duct obstruction.

The Effect of Fractional Dosage in the Administration of Exogenous Bile Acid as a Test of Shunt Patency.—As was reported in the previous paper,[1] in certain situations the patent shunt experiment can be made to yield peripheral bile acid curves which are defined by relatively low and prolonged peripheral bile acid elevations. Such a situation exists if the cholic acid is administered in a capsule in one dose. Slow dissolution of the capsule delays the absorption of the contents and the resultant elevations of peripheral total bile acids are low and delayed in their occurrence. This is contrasted with curves obtained after administering the bile salt through an indwelling duodenal tube, such curves having the desirable sharp rise, high peak, and rapid fall. These observations were in part confirmed by our early clinical application of this test to patients who had recently had a portacaval shunt. The first tests were performed by giving the patients 10 capsules in one dose: each capsule containing 5 gr. of ox bile. The resultant curves were low and subject to indecisive interpretation. At that time, clinical tests were not made by introducing the cholic acid through an indwelling duodenal tube. However, the desirability of introducing the bile salt orally rather than by intubation is evident, and therefore animal experiments were conducted using fractional oral doses of cholic acid.

Experiments.—Side-to-side portacaval shunts were constructed in one group of three dogs and Eck fistulas in another group of four dogs. After recovery from the operation, cholic acid (150 mg. per kilogram of body weight) was divided into 3 equal doses in capsules. The 3 capsules were ad-

ministered orally with small amounts of meat at thirty-minute intervals. Blood sampling was made at one-half, one, three, and five hours after the final dose of cholic acid. In all such experiments testing either type of shunt, the resultant curve was similar to that obtained by introducing the cholic acid dose through an indwelling duodenal tube. Fig. 2 is a representative curve from seven such experiments.

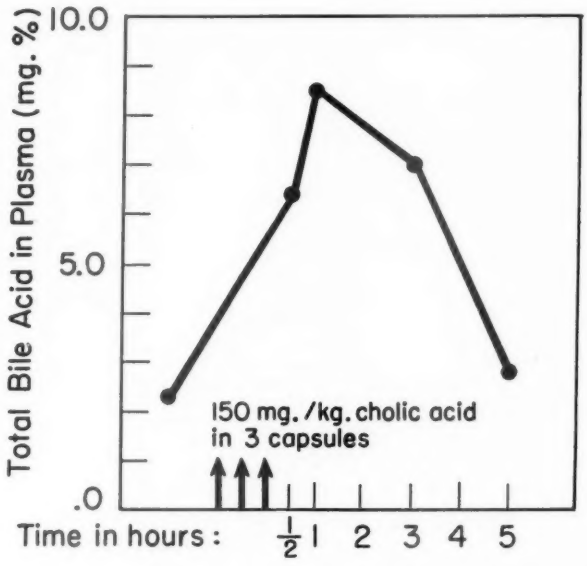

Fig. 2.—Total bile acid in peripheral blood after divided oral administration of cholic acid in shunted dogs. Average of 7 experiments.

DISCUSSION

It is evident that application of the enterohepatic circulation of bile acids as a test for the patency of a portacaval shunt is subject to the previously mentioned factors: (1) the rate of absorption of bile acid from the intestine; (2) the functional patency of the shunt; and (3) the rate of disappearance of the bile acid from the blood.

The first factor concerns the manner in which the enterically administered cholic acid is introduced into the cycle of bile acid circulation from the liver to the bowel and back to the liver. Evidence is presented that the cholic acid may be introduced in one dose through an indwelling duodenal tube or in oral capsules in divided doses at thirty-minute intervals. In the presence of a patent shunt, the resultant rise in peripheral total bile acids is significant and subject to correct interpretation. However, if the cholic acid is given orally in one capsular dose, the rise in peripheral total bile acid is either not observed or occurs at a delayed interval, and is of a low magnitude.

One of us (C. G. J.) and others[4, 5] have pointed out the fact that the elevation of the bile acid concentration in the peripheral circulation is observed after administration of exogenous bile acid in man and in the hog with biliary obstruction. Since our previous experiments on portacaval shunts were made on dogs, the experiments on acute biliary obstruction were again repeated,

this time also on dogs. The previous observations were confirmed and the elevations of peripheral total bile acids found to have three characteristics different from those occurring in a patent shunt. These were a delay in the occurrence of the peak elevation, a significantly higher peak elevation, and a sustained elevation in the circulation for a period of ten hours or more.

We have had an opportunity to apply this test to two patients with newly constructed side-to-side portacaval shunts.

CASE 1.—G. T., a 59-year-old white man, was admitted to the hospital with a chief complaint of gross hematemesis and melena for one day. The past history indicated a heavy alcoholic intake for forty years and ankle edema for the past six months. There was no previous hemorrhage and no history of jaundice. Examination revealed a blood pressure of 106/60, and the skin presented no jaundice or spider nevi. The liver was palpably enlarged. The clinical diagnosis was portal cirrhosis with bleeding esophageal

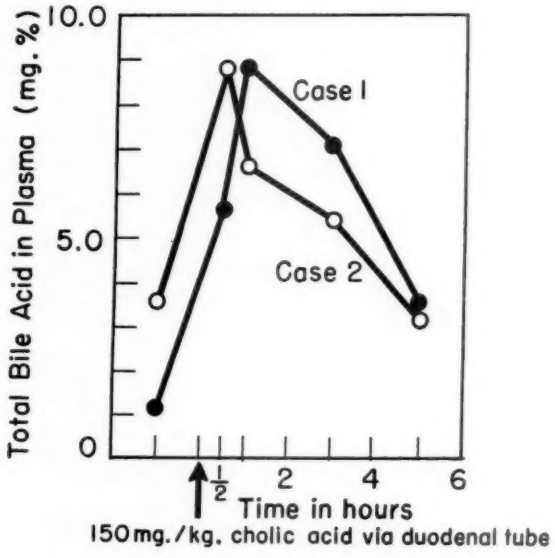

Fig. 3.—Clinical observations: rise in peripheral blood total bile acid following side-to-side portacaval anastomoses.

varices. The hemorrhage ceased spontaneously without benefit of esophageal tamponade and, after 1,500 c.c. whole blood transfusion, the hemoglobin was 12.2 Gm. The Bromsulphalein retention was 11 per cent, whereas the serum proteins and serum bilirubin were normal. One week after admission, roentgenographic examination of the esophagus revealed no esophageal varices. Subsequently, esophagoscopy was negative for the visualization of varices.

At operation, a cirrhotic liver was found. There was no ascites and portal pressures were found to be 380 mm. of water. No duodenal pathology was demonstrable. The hemorrhage was believed due to esophageal varices secondary to portal cirrhosis, for which reason a side-to-side portacaval shunt was performed. The postoperative course was satisfactory, and two weeks after operation a solution containing 150 mg. per kilogram of body weight of sodium cholate was administered through a duodenally placed tube over a period of ten minutes. Cubital vein blood samples taken at one-half, one, three, and five hours after duodenal administration of bile salt revealed a moderate elevation of total bile acid as compared with a control (Fig. 3). Such an elevation is regarded as indicative of a patent shunt.

CASE 2.—A. B., a 53-year-old white man, was admitted to the hospital with a chief complaint of hematemesis for one day and melena for one week. The past history consisted of one previous episode of upper gastrointestinal hemorrhage following an attack of acute alcoholism. Subsequent roentgenographic studies revealed no peptic ulcer or esophageal varices. Examination revealed a poorly nourished white man with slight icterus and a palpably enlarged liver. The hemorrhage continued unabated and the day after admission a gastrotomy was performed which was negative. The liver was cirrhotic and ascites was noted. Immediately thereupon a transthoracic obliteration by suture of large esophageal varices was made. The postoperative course was satisfactory and further laboratory work revealed a Bromsulphalein retention of 33 per cent and serum albumin of 2.7 mg. per cent with a serum globulin of 3.4 mg. per cent. Esophageal bleeding recurred and was controlled with a balloon tamponade. After further supportive preparation over a six-week interval, a side-to-side portacaval shunt was performed, with a satisfactory postoperative course. On the twelfth postoperative day a bile acid circulation test was made in which a solution of sodium cholate (cholic acid 150 mg. per kilogram of body weight) was administered slowly through a doudenal tube over a period of fifteen minutes. Blood samples were again taken from the antecubital vein at one-half-, one-, three-, and five-hour intervals after administration of the cholate. There was a moderate elevtion in the concentration of peripheral total bile acids observed (Fig. 3). This was interpreted as indicative of a patent shunt.

SUMMARY

1. Experiments are described which relate the rise in peripheral total bile acids, after enteric administration of cholate in a dog with a portacaval shunt, to the method of administration of the cholate.

2. The relation of the elevations of peripheral total bile acids, following acute bile duct obstruction in dogs without shunts, is compared with those observed in the shunted animal.

3. Two clinical cases with recently constructed portacaval shunts were subjected to bile acid circulation studies. In both cases there was a significant rise in peripheral total bile acids following the administration of cholate in an indwelling duodenal tube. These studies were interpreted as indicating that the shunts were patent.

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EVALUATION OF ORLON FABRIC IN THE REPAIR OF DEFECTS IN THE ABDOMINAL WALL

Effect of Infection on the Fate of Orlon Implants and Simultaneous Comparison With Tantalum Gauze

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A VARIETY of prostheses have been used to facilitate the repair of large tissue defects.[1-5] Tantalum gauze has proved the most satisfactory material for the bridging of musculofascial defects to date; however, it is still not without disadvantages.[6] Recently, synthetic fabrics, such as Vinyon "N"[7] and Orlon[8] have been used extensively as experimental and clinical vascular grafts, and their function appears to be quite satisfactory. Other synthetic fabrics, Fortisan[4] and nylon,[5] have been found satisfactory for the repair of musculofascial defects in the absence of infection.

The course of infection in the presence of foreign materials implanted into tissue is a major factor in determining the final usefulness of such prostheses. Tantalum has been reported to cause "no trouble whatsoever, unless there is some other nonabsorbable foreign body present with the tantalum."[6] Fortisan, when contaminated, has been found to result in abscess formation with persistent sinuses or buried granulomata.[9] When inserted under sterile conditions, Orlon fabric was relatively inert and functioned well in the bridging of defects in the abdominal wall or in the hemidiaphragm of the dog.[10] To extend these observations, the effect of infection on the fate of Orlon was evaluated. This included the simultaneous comparison of Orlon fabric and tantalum gauze in the same animal, both in the presence and absence of infection.

METHODS AND MATERIALS

Orlon, an acrylonitrile derivative, is resistant to acid, alkali, and organic solvents. The fabric used was purchased locally from a department store. It was made up of twisted strands 100 denier in size with 88 by 72 strands to the inch. Squares measuring 2.5 by 2.5 cm. and 5.0 by 5.0 cm. were sewn with 0.3 cm. hems on all four sides using Orlon thread. The implants were washed with acetone and alcohol, then with a commercial detergent (Tide), rinsed well, and sterilized by boiling.

The tantalum gauze was made up of 0.0024 gauge monofilamentous strands with 51 by 51 strands to the inch. Squares measuring 2.5 by 2.5 cm. were used without turning the edges under to form hems. These were washed and sterilized in the same manner as the Orlon.

Rabbits were used in preference to dogs in all the experiments since ventral hernias are difficult to produce in dogs, even in the presence of relatively large musculofascial defects.[1, 9] Rabbits have a proportionately large abdominal wall, which suggested that they might be more suitable for the functional evaluation of a prosthesis such as Orlon fabric.

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Two surgical procedures were carried out; one was used in the first phase of the study, the other in the second phase. All procedures were performed using sterile technique in an operating room. In the first phase a full-thickness defect in the abdominal wall was produced. A midline incision was made at the midabdominal level; then a 5.0 by 5.0 cm. defect created by removing the full thickness of the abdominal wall except for the skin. The Orlon implant was sutured in place with a continuous 00 chromic catgut suture and reinforced with interrupted catgut sutures at the corners. The subcutaneous tissues and skin were closed as a single layer with a continuous 00 chromic catgut suture. In control animals, a 5.0 cm. transverse incision was made through the muscles and peritoneum and closed with 00 chromic catgut. In other respects, the operation was similar to the one involving Orlon implantation.

In the second phase of the study, Orlon fabric and tantalum mesh were compared in the same animal. Bilateral vertical incisions were made about 2.0 cm. lateral to the nipple lines at an upper midabdominal level. Squares of Orlon and tantalum measuring 2.5 by 2.5 cm. were sutured to the external abdominal oblique muscles using interrupted sutures of 00 chromic catgut at the four corners. The skin was then closed with a continuous 00 chromic catgut suture. Implants were placed bilaterally to avoid variations in postoperative edema which might alter the degree of infection.

Infection was produced in a uniform, reproducible manner. A strain of *Staphylococcus aureus,* coagulase positive, phage type 44-A, or a strain of *Aerobacter aerogenes* was grown in broth culture medium for eighteen hours, then centrifuged and washed twice with isotonic saline solution to remove broth and toxins. Suspensions of either or both organisms in saline solution containing a known concentration of bacteria, were pipetted onto the Orlon, tantalum, or control site just prior to closing the laparotomy wound. The 5.0 by 5.0 cm. Orlon squares were inoculated with 64-357 $\times$ 10^6 bacteria, while the 2.5 by 2.5 cm. implants were inoculated with 18-93 $\times$ 10^6 bacteria per implant.

Those animals in which Orlon alone was evaluated were followed with daily examinations, daily rectal temperatures, leukocyte counts twice weekly, blood cultures, and wound cultures when clinically indicated. No antibacterial therapy was given. The wounds were not drained surgically at any time during the course of infection. Four animals (one "Orlon control," one "infection control," and two with "Orlon and infection") were reoperated upon eight days after the initial operation and were reinfected. Likewise, secondary closure of open infected wounds was attempted twenty-two days postoperatively in four animals. In no other instances was secondary surgical closure of draining wounds attempted.

RESULTS AND DISCUSSION

The Effect of Infection on the Fate of Orlon.—An evaluation of Orlon fabric in the repair of large (5 by 5 cm.) full-thickness defects both in the presence and in the absence of infection was based upon studies in 26 animals (Table I).

TABLE I. EFFECT OF INFECTION UPON THE FATE OF ORLON

EXPERIMENTAL PROCEDURE	NO. OF ANIMALS	DURATION OF STUDY (DAYS)	FEVER	COMPLICATIONS*					SATISFACTORY	UNSATISFACTORY
				DEHISENCE		HERNIA	ADHESIONS	ABSCESS†		
				CLOSED	SINUS					
Orlon control	4	43-57	1/4		1/4	0/4	3/4	0/4	2/4	2/4
Infection control	4	43-57	3/4	2/4	0/4	1/4	0/4	0/4		
Orlon and infection	18‡	22-93	9/14	0/14	6/14	2/14	11/14	9/14	3/14	11/14§

*Number per total number.

†Abscesses present at the time of sacrifice.

‡Four animals dying of bacteremia in less than 14 days were excluded from tabulation of complications.

§Orlon sloughed out of two animals.

The usefulness of Orlon fabric in the absence of infection was studied in four animals which were not intentionally contaminated at operation (Orlon

controls). However, one of these became infected after being reoperated upon eight days following the original procedure. In the remaining uncontaminated animals there was no fever, no evidence of suppuration, and the wounds healed well. Adhesions developed between the Orlon, the omentum, and bowel in three animals. The implants remained quite smooth and were well infiltrated with fibrous tissue in two animals. While the group was small, except for the occurrence of adhesions, the Orlon fabric seemed satisfactory in the absence of infection (Fig. 1), thus substantiating the previous observations in dogs.[10]

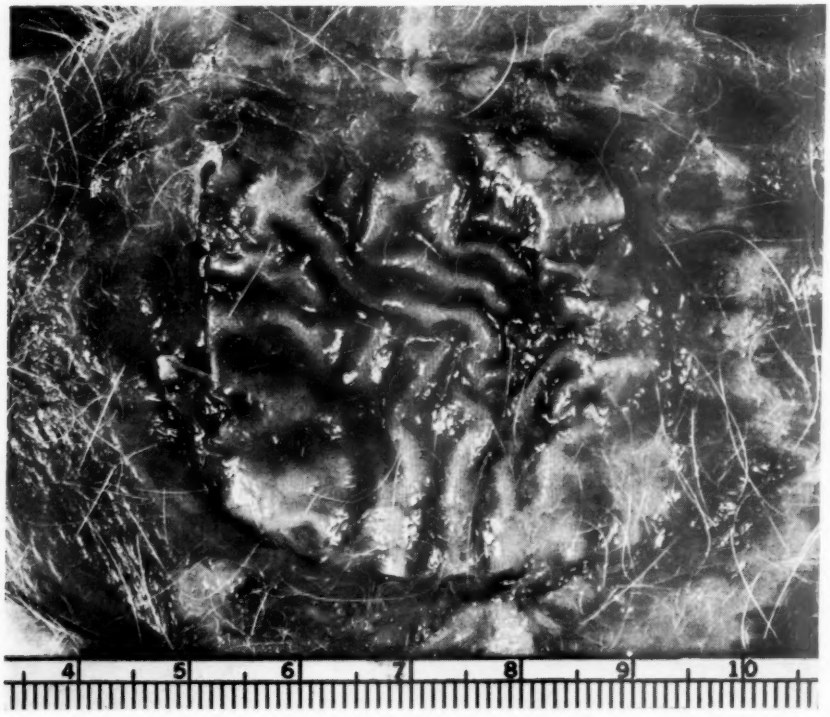

Fig. 1.—The appearance from the peritoneal surface of a full-thickness noncontaminated Orlon implant in the abdominal wall of a rabbit (No. 267) 43 days postoperatively. Note the glistening surface and the minimal wrinkling (original implant was 5 by 5 cm. in size).

The effect of bacterial contamination on the healing of abdominal wounds which were closed primarily and did not contain Orlon fabric was studied in another group of four rabbits (infection controls). Three of the four animals were febrile postoperatively. Large abscesses developed in two animals; these drained spontaneously on the eighth day and went on to close by the nineteenth and twentieth days. A third animal developed a ventral hernia on the twenty-ninth postoperative day which measured 7 by 7 cm. at the time of sacrifice.

The effect of infection on the usefulness of Orlon fabric was studied in a third group (Orlon and infection), which was made up of 18 animals. The Orlon was contaminated at operation with either *Staph. aureus, A. aerogenes,* or a mixture of both species of bacteria. Four animals in this group died of overwhelming infection during the first two weeks. They were excluded from the tabulations.

The findings in the remaining 14 animals were of interest. Wound abscesses, excluding minor infections about sutures, developed in 11 animals. In the animals infected with *Staph. aureus* the wounds tended to remain closed; however, by the third week subcutaneous nodules (about 3 by 3 cm. in size) were present at the sites of Orlon implantation. The wounds infected with *A. aerogenes* or those with mixed infection began to drain during the second week. Six of the 14 developed draining sinuses which persisted until time of

Fig. 2.—Large ventral hernia, such as were noted in three animals (one was an infection control and two had contaminated Orlon). This animal (No. 231) developed a draining sinus, following contamination of the Orlon. In this instance the Orlon implant had sloughed out by the time of sacrifice (57 days). Note the persistent draining sinus.

sacrifice (93 days postoperatively in two instances). The Orlon implants sloughed out of the wounds in two of the animals which developed draining sinuses. In no instance, even after the Orlon had sloughed, did a sinus tract close spontaneously. Large ventral hernias developed in two animals, one of which had previously sloughed the Orlon implant (Fig. 2). Adhesions between Orlon implant, bowel, omentum, or bladder were uniformly present (11 of 14 animals). Most of the adhesions had to be separated with sharp dissection.

At the time of sacrifice large fibrous-walled abscesses were found in nine animals. The fibrous capsule was very firm and measured 2.0 to 3.0 mm. in thickness. Upon opening these abscesses, the Orlon was found matted and ly-

ing free in cavities filled with pus (Fig. 3). Organisms of the species originally inoculated into the wounds were present when the abscesses were cultured. The Orlon implant in every instance was intact and could be spread out to its original size of 5.0 by 5.0 cm. In the infected animals only three of the Orlon implants were satisfactory, although one of these had small suture abscesses at the four corners. These three implants were well infiltrated with fibrous tissue and could be removed from the surrounding tissue only with extreme difficulty.

Fig. 3.—Fibrous-walled abscess cavity, from the peritoneal surface, opened to show matted Orlon and pus (No. 474, 43 days postoperatively). The Orlon was shelled out of the lower half to show thick-walled fibrous cavity.

Microscopic study of representative tissues from each of the three groups of animals confirmed the observation that Orlon fabric elicited only a minimal foreign body response in the absence of infection. The observation of marked fibrosis and abscess formation noted upon gross examination was confirmed by microscopic studies.

Comparison of Orlon With Tantalum.—Koontz and Kimberly[11] had noted satisfactory healing in five of ten animals (dogs and rabbits) when infection developed in association with tantalum implants. Our poor results with Orlon implants may have been the result of a more severe infection. Thus, a comparison of tantalum mesh with Orlon fabric under similar experimental conditions seemed necessary.

Both Orlon fabric and tantalum mesh were sutured to the anterior sheath of the external abdominal oblique muscles, one being placed on each side of

the animal. The order was reversed as each animal was done. The prostheses served no function in these animals; however, they were satisfactory for a comparison of the effects of infection.

Evaluation, as in the first series, was based upon frequent examination during the postoperative course and upon gross pathologic findings at the time of sacrifice. In six animals followed from 112 to 131 days postoperatively, roentgenograms of the abdominal wall were examined for evidences of calcification. In addition, the occurrence of wrinkling in an implant appeared undesirable and was often associated with an excessive amount of scar tissue. The tantalum gauze and Orlon fabric implants had areas of 6.25 sq. cm. when implanted. Comparison of the original area with the area measured at sacrifice gave an objective indication of the wrinkling and contraction that occurred.

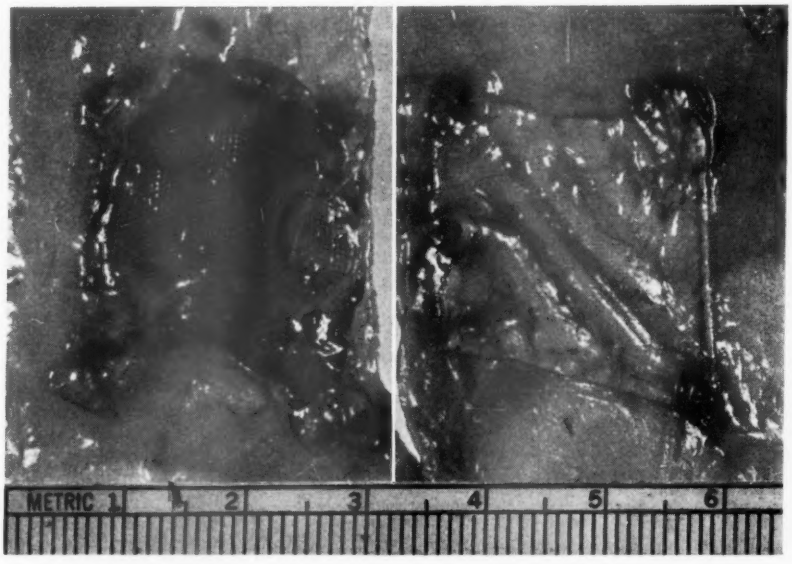

Fig. 4.—Comparison of a tantalum gauze (left) and an Orlon fabric implant (right) in the absence of infection (No. 835, 43 days postoperatively). Note the suture granulomata at the four corners, the small blood vessels traversing the implants, and the minimal wrinkling of both implants.

A comparison of the two materials in the absence of infection was made in eight animals (Table II). Suture granulomata were present at the four corners of each implant in the two animals studied 43 days postoperatively. These were due to the use of chromic catgut, hence, not considered as complications. Both materials served quite satisfactorily in the absence of infection, although nonintentional infection developed in two animals. Abscesses were found involving one of the Orlon and one of the tantalum implants. No evidence of calcification involving the Orlon fabric or tantalum mesh was noted. All implants were quite smooth and well infiltrated with fibrous tissue (Fig. 4).

A simultaneous comparison of the tissue reactions to Orlon fabric and to tantalum gauze in the presence of infection was made in 16 animals (Table II). The implants were contaminated at the time of operation with the same

strains of bacteria as were used in the studies with Orlon alone. One animal died on the ninth day and was not included in the final evaluation.

TABLE II. COMPARISON OF ORLON WITH TANTALUM

EXPERIMENTAL PROCEDURE	NO. OF ANIMALS	DURATION OF STUDY (DAYS)	COMPLICATIONS OF INFECTION						COMPARISON OF IMPLANTS		
			ORLON			TANTALUM			ORLON SUPERIOR	EQUAL	TANTALUM SUPERIOR
			SINUS	ABSCESS	AREA†	SINUS	ABSCESS	AREA†			
Noninfected	8	41-131	0/8	1/8	4.0	1/8	1/8	4.1	1/8	4/8	3/8
Infected	16*	28-55	4/15	11/15	2.4	0/15	3/15	5.2	0/15	0/15	15/15

*One animal excluded which died on the ninth postoperative day.
†Area in square centimeters.

The tantalum gauze showed only questionable predisposition for enhancement of infection. During the postoperative course the tantalum implants remained flat to palpation. Draining sinus tracts did not develop. At the time of sacrifice subcutaneous abscesses were noted in three animals. The degree of wrinkling of the tantalum implants was minimal. The average area at the time of sacrifice was 5.2 sq. cm. All implants were well infiltrated with fibrous tissue.

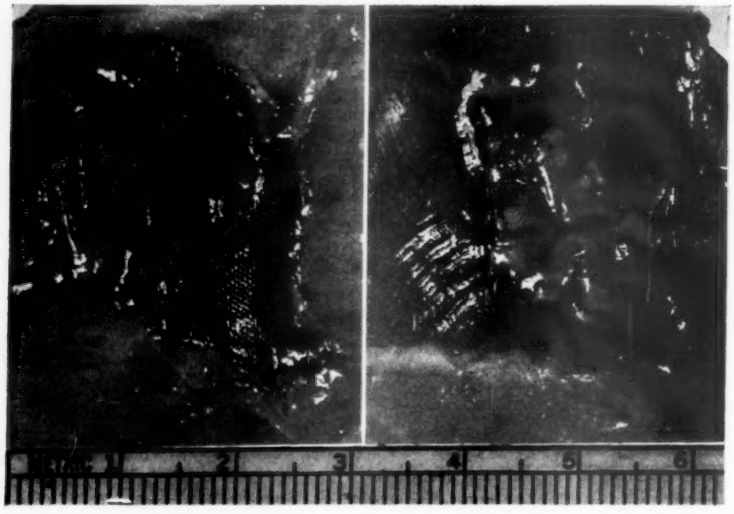

Fig. 5.—Comparison of a tantalum gauze (left) and an Orlon fabric implant (right) in the presence of infection (No. 908, 41 days postoperatively). Note the moderate wrinkling of the Orlon implant. There was a small amount of pus beneath this Orlon implant.

The Orlon implants, on the other hand, showed the same marked predisposition for enhancement of infection shown in the earlier studies. During the second week after operation the Orlon implants uniformly began to feel nodular. Draining sinuses developed in 4 of 15 animals. At the time of sacrifice the Orlon in all instances was found to be wrinkled, varying in area from 1.0 to 4.0 sq. cm. with a mean area of 2.4 sq. cm. The wrinkled Orlon in 11 animals was covered by a fibrous capsule which was quite strong. If the capsule was incised, the Orlon could be removed with little difficulty from the surrounding tissue. Fibrous tissue had not uniformly infiltrated the Orlon fabric. Pus

was present in six of these fibrous cysts (abscesses), while five contained none. The remaining four Orlon implants were quite well infiltrated with fibrous tissue in spite of the marked wrinkling (Fig. 5).

The tantalum gauze was considered superior to the Orlon fabric in all 15 animals which had been inoculated with bacteria. The tantalum mesh only rarely predisposed to the development of chronic infection if contaminated, whereas contamination of the Orlon fabric uniformly resulted in chronic infection.

In the repair of many large hernias there is a risk of the wound becoming infected because of the nature of the skin and underlying tissues through which the surgeon must operate and the degree of dissection required. The usefulness of Orlon fabric as a prosthesis in the repair of musculofascial defects would thus seem limited. These findings are in complete accord with the observations made on another synthetic fabric, Fortisan, when infection developed.[9] This may suggest that other similar types of synthetic fabrics, while relatively inert from the standpoint of tissue reaction in the normal host, may predispose to the development of chronic infection if bacterial contamination occurs.

SUMMARY

1. Rabbits are satisfactory experimental animals in which to study prostheses for the repair of musculofascial defects in the abdominal wall, as they may develop ventral hernias and respond in a relatively uniform fashion to a standard infection.

2. The usefulness of Orlon fabric as a prosthesis in the repair of musculofascial defects seems limited. Following contamination, the wound in which Orlon fabric is present uniformly goes on to chronic infection with the frequent formation of abscesses and draining sinuses.

3. Tantalum mesh does not predispose to the development of chronic infection following standardized contamination of a wound.

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HOMOTRANSPLANTATION OF THE CANINE LIVER

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IN THIS communication we shall report our experience with homotransplantation of the dog's liver. Our purpose in attempting this transplantation was, first, to find out whether the operation was technically possible with survival of the liver, and, second, to determine the longevity of such transplants and their effect upon the host. The dual blood supply of the liver presents a unique technical problem for which we developed several types of anastomoses. A greater difficulty, however, is the sensitivity of this organ to anoxia.[1] This obstacle is compounded in the dog by the presence of intrahepatic saprophytic clostridia which proliferate rapidly under anaerobic conditions. These organisms cannot be uniformly eliminated although Raffucci and Wangensteen[2] have demonstrated an increased tolerance to interruption of hepatic arterial flow in dogs prepared with wide-spectrum antibiotics.

In the experiments being reported, we attempted to ameliorate the effects of hepatic anoxia during the period of complete interruption of liver blood flow while transplanting the organ by two methods. We first used long-term preparation of the donor with wide-spectrum antibiotics, in an attempt to eliminate the intrahepatic saprophytes. Later, we inserted a polyethylene shunt between the recipient dog's aorta and the hepatic arterial tree of the donor liver while performing the afferent anastomoses. This latter technique proved more satisfactory and will be described in detail.

EXPERIMENTAL METHOD

Technique of Liver Transplantation Using an Arterial Shunt.—Donor and recipient dogs were prepared simultaneously by two surgical teams, and the entire liver of the donor was transplanted with the accompanying vascular trunks into the lower abdomen of the recipient. The recipient's liver was not disturbed. Donor animals were selected so that they weighed 5 to 10 kilograms less than the recipients. Intravenous Nembutal anesthesia was used and the donor was carried on endotracheal intermittent positive pressure.

By careful dissection the donor's portal vein, infrahepatic and suprahepatic vena cava, and the hepatic artery and its proximal tree were isolated via a thoracoabdominal incision. Since the hepatic artery was usually too small for reliable patency of the anastomosis, it was usually necessary to use the celiac axis or a segment of aorta. With the other branches ligated, the aortic segment provided a readily anastomosed extension of the donor's hepatic artery. Before removing the liver, the donor was heparinized.

At the same time, the recipient's vessels were prepared through a lower right rectus abdominal incision. The infrarenal inferior vena cava, the distal aorta, and external iliac arteries were isolated. The vena cava was transected and fixed over a Blakemore-Lord cuff,[3]

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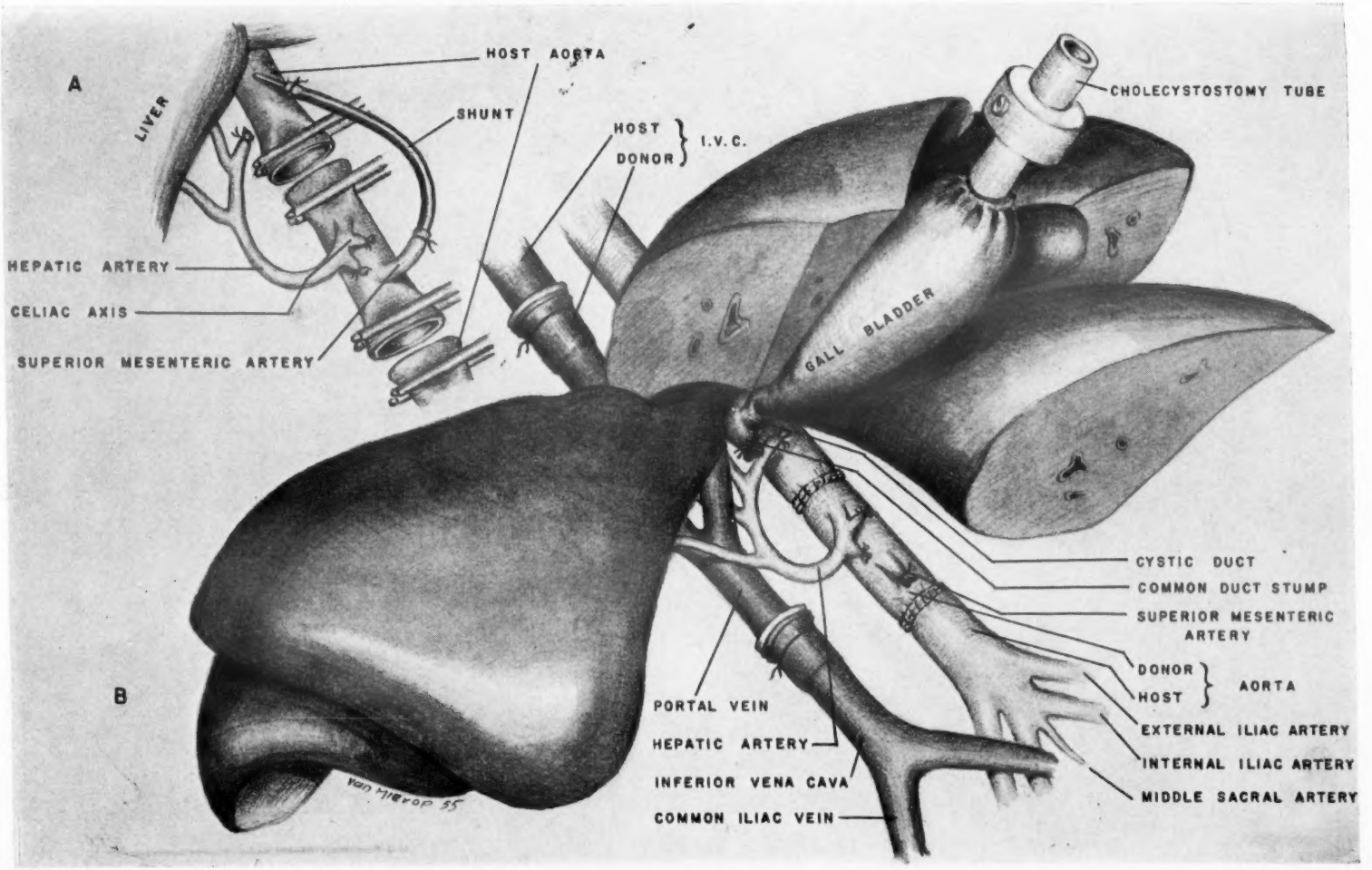

Fig. 1.—*A*, Demonstrates the temporary shunt between the recipient dog's aorta and the donor liver. The course of arterial blood flow from the recipient's aorta is via the polyethylene shunt to the superior mesenteric artery and aortic segment of the transplant. *B*, Demonstrates the completed liver transplant and shows the afferent and efferent anastomoses as described in the text.

in preparation for nonsuture anastomosis to the subcardiac vena cava of the donor. The site of transection of the aorta was then elected, and a polyethylene tube was inserted into this vessel in a position proximal to the level of transection.

When the recipient had been prepared, the donor's vessels were transected as rapidly as possible, in the following order: the infrahepatic vena cava which was ligated, the portal vein, the aorta below and above the celiac axis, and the subcardiac vena cava. The liver was then placed in the lower abdomen of the recipient and the hepatic outflow was first established by completing the vena cava anastomosis over the previously placed Blakemore-Lord cuff. The polyethylene shunt was then connected to another tube placed in a branch of the hepatic arterial tree of the donor liver. When using the aortic segment preparation, the superior mesenteric artery proved to be the most suitable location for the shunt. With the shunt in operation, it was then possible to perform both proximal and distal aortic anastomoses accurately and less hurriedly, meanwhile being assured of adequate oxygenation of the transplanted liver. When the arterial anastomoses were completed, the shunt was discontinued and the portal vein of the donor was connected to the recipient's distal vena cava over a second Blakemore-Lord cuff. To prevent motion of the transplant and kinking of the suprahepatic vena cava, the diaphragmatic tags on the suprahepatic vena cava were tacked to the right psoas fascia with one or two sutures. Finally, a plastic cholecystostomy cannula* was inserted and brought out through the wound, which was then closed in layers. Fig. 1 is a diagrammatic representation of the liver transplant with anastomoses.

Liver biopsies were obtained before and after transplantation and at daily intervals after operation. Bile output was recorded and in some animals daily Bronmsulphalein extraction curves were obtained. The clinical condition of the animals was closely followed and antibiotics, fluids, and blood were given as indicated. Upon death or sacrifice post-mortem examinations were performed.

Other Techniques for Liver Transplantation.—The technique described here was developed after a number of other methods had proved less satisfactory. Arterialization of the donor's portal vein by the recipient's external iliac artery, after the method of Schilling, was first used.[4] In these experiments the hepatic arterial tree was not used. Later, end-to-end anastomosis of the recipient's external iliac artery to the donor's hepatic artery or celiac axis was combined with anastomosis of a recipient common iliac vein to the donor portal vein. All of the animals in the earlier experiments were prepared with oral wide-spectrum antibiotics† for periods ranging between four and twenty-one days, in an attempt to prolong the hepatic tolerance to anoxia. No shunt was used in these experiments. Animals in this group were followed postoperatively in the manner outlined previously.

RESULTS

Survival of Transplants.—Homotransplantation of the canine liver has been performed successfully twenty-one times in forty-nine attempts. In all successful cases the animals lived at least five days, and in no unsuccessful experiment did the recipient survive over thirty-six hours. In all successful experiments, bile was produced for from one to seven days with one exception, in which viable hepatic tissue was demonstrated by needle biopsy on the first postoperative day. In five of the animals having successful transplants, removal of the recipient's liver was performed on one of the days following transplant. None of the recipients survived this procedure. The shunt technique as described was used in thirteen pairs of animals with 69 per cent successful transplantations, while in thirty-six pairs of animals prepared with wide-spectrum antibiotics and having various types of afferent anastomoses there was 33 per cent survival.

*Manufactured by Mr. L. W. Carson, Wheaton, Ill.

†The chlortetracyclene and tetracyclene used in these experiments were supplied by Lederle Laboratories, Division of American Cyanimid Company.

Typically, in a successful transplant experiment, bile began to rise in the cannula as the wound was being closed. The animals recovered from the anesthesia within one to four hours, but remained lethargic for from twelve to twenty-four hours. During the first day bile was produced at a rate of 2 c.c. per kilogram of donor body weight. Solid food was occasionally taken at this time, but more frequently the diet was voluntarily limited to liquids. The temperature and pulse rate were normal or slightly elevated, but no local signs of peritoneal irritation were manifested when omentum was draped over the liver prior to closure. By the end of the second day, bile output increased, and the animal appeared to be approaching a more nearly normal state. During the third twenty-four-hour period, bile secretion by the transplant was usually maximum and amounted to 4 to 5 c.c. per kilogram of donor weight. During this period the bile was very dark, mucoid, and rather typical of gall-bladder bile. In the subsequent two days, the bile output fell off and the bile became less intensely colored and more watery. About the fifth day secretion ceased and was followed in one or two days by a serosanguineous, then a foul sanguinopurulent discharge via the cholecystostomy cannula. After the fifth day survivors exhibited varying degrees of toxemia which were frequently fatal, and exploration after cessation of the bile flow revealed a completely necrotic liver, usually infected, in the process of degeneration and sloughing.

Microscopic Studies of Liver Biopsies.—The microscopic picture of the transplanted liver usually correlated well with the bile output, although occasional inconsistencies were found. These were thought to be due to failure of some portions of the transplant to receive an adequate blood supply while other portions of the organ were functioning. Liver biopsy taken immediately after transplantation showed morphologic changes of varying intensity. In practically every instance there was some sinusoidal congestion which seemed to extend peripherally from the region of the central vein, and in extreme cases this congestion caused disruption of the hepatic cords. Where frank necrosis of individual hepatic cells occurred, it was usually centrolobular and was accompanied by a polymorphonuclear leukocytic infiltrate. When the experiment terminated within thirty-six hours, a wide range of microscopic changes were found, ranging from a slight progression of these changes to massive necrosis with bacterial invasion and intense acute inflammatory exudate. Both needle biopsies and sections of successful transplants taken at exploration or autopsy showed a patchy distribution of lesions. Serial biopsies, therefore, sometimes exhibited rather marked differences, with relatively badly damaged tissue being followed the next day by a specimen exhibiting relatively minor change. When viewed as a group, however, the pattern of change was fairly constant. In some of the surviving animals slight recovery from the congestion and cellular changes seen immediately postoperatively was found. In no instance, however, did the liver ever regain its control status. In a few instances focal anemic necrosis associated with congestion and hemorrhages with acute inflammation progressed rapidly so that the liver was more or less totally destroyed by the second or third day.

Usually, however, beginning on the fourth day, there was more or less general increase in cellularity of the portal spaces. The exudate consisted of numbers of small round cells of the chronic inflammatory type and larger mononuclear cells, presumably fibroblasts. This reaction continued in a progressive fashion. At about the same time, rather extensive necrosis of the remaining hepatic tissue occurred. This was usually patchy in distribution but eventually became generalized. In the end, the liver was totally necrotic and all anatomic features were lost. In only one animal was any viable tissue seen after the sixth postoperative day. In this particular instance, moderate amounts of apparently viable tissue were found about the periphery of the lobules, whereas the central portion showed extensive anemic necrosis, congestion, and acute inflammatory infiltrate. This animal died of distemper on the seventh day.

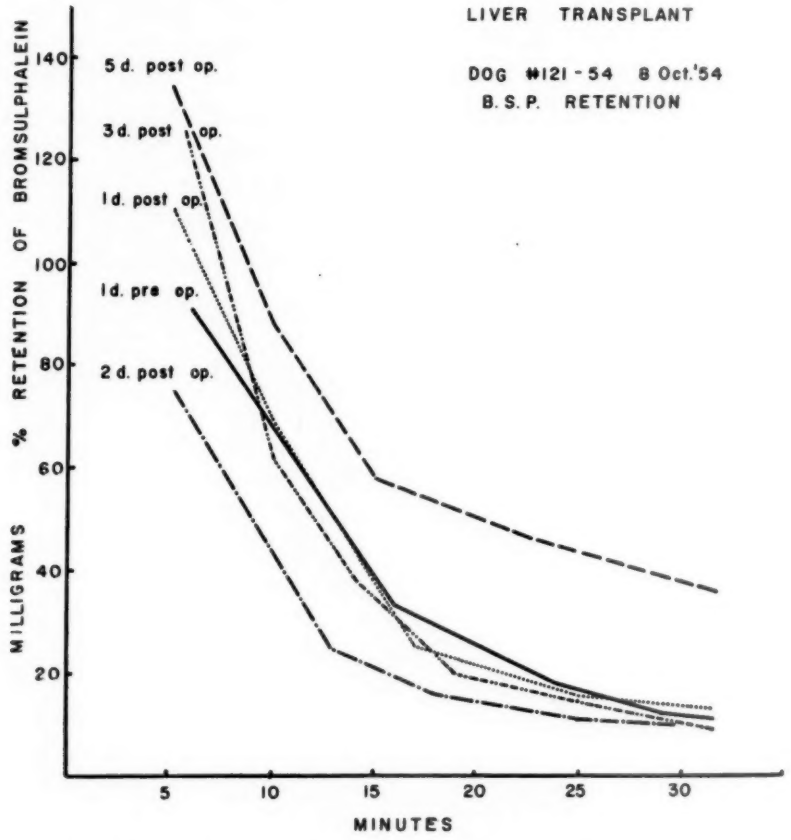

Fig. 2.—The values for Bromsulphalein retention in the serum of a dog in whom a liver transplant is functioning are shown above. Five milligrams per kilogram of the combined weights of both dogs (recipient and donor) was given. The curve designated 1 d. preop. is the control. Curves on the second and third postoperative days show that a more rapid extraction of the dye occurred, the result of the additive function of the liver transplant. On the fifth day dye extraction was less than normal. At this time the transplant was nonfunctioning.

Bromsulphalein Extraction.—Bromsulphalein extraction curves obtained on five survivors also correlated with bile production and the microscopic picture, indicating maximal transplant function on the third day. In Fig. 2, extraction curves for Bromsulphalein taken in one experiment are shown.

Complications.—Occlusion of the venous return from the hindquarters in the early experiments caused edema in several animals, and the development of abdominal collaterals increased the hazard of needle biopsy. Therefore, direction of the venous return from the legs through a portal vein of the donor liver was effected in perfecting the transplantation technique. A few cases of right hindlimb paralysis were precipitated by interruption of the right external iliac artery, but this complication did not develop in those animals in which the distal circulation was re-established.

Employment of the shunt technique doubled our survival rate and reduced the necessity for completing the arterial anastomosis hurriedly, thereby reducing the incidence of thrombosis. It also obviated the labor and expense of prolonged preoperative preparation of the donor in an uncertain attempt to render the liver bacteriologically inactive.[5] The shunt was found to require constant attention during anastomosis. On several occasions the vessels of the transplant became twisted about the end of the relatively rigid shunt, causing premature thrombosis within the tube, and quite possibly within the artery, also.

Of the twenty-eight transplantations which were failures, eight were due to what can be called, for lack of a better term, "toxemia."[6, 7] In six of these the liver was completely anoxic for over thirty minutes, and in three gross gas bubbles were encountered in the liver at post mortem. In no case did the recipient survive when the donor liver was anoxic for over thirty-three minutes. Afferent arterial anastomosis thrombosis caused eight failures when arteries smaller than the aorta were used, although one liver secreted 15 c.c. of bile for six hours before death. Intraperitoneal hemorrhage caused four deaths. In two instances the efferent vena caval anastomosis was twisted, causing multiple fractures in the dome of the liver, while in one case a dehiscence occurred at the portal iliac vein cuff anastomosis. No source of hemorrhage was established in the other animal. Aspiration of gastric contents caused one death, and in one experiment the animal died of a massive pulmonary embolism after release of the vena caval clamp. The occluding clamp had been placed about 3 cm. below the highest point of dissection on the vena cava, contrary to our usual practice, and had thereby allowed a thrombus to form between the clamp and the renal vein. No cause of death could be determined in five cases.

DISCUSSION

Homotransplants of kidneys in animals have been shown to survive for from one to eighteen days, with the majority of investigators reporting an average of four days of transplant function.[8] These organs are then destroyed by the inevitable host reaction which is thought to be an immunologic phenomenon.[9] We have been able to demonstrate that the liver can be transplanted with maintenance of viability for varying periods up to one week. It would appear, therefore, that the canine liver is subject to the same forces which govern the course of renal homotransplants in this species. Of great significance is the finding of Hume and associates[8] that homotransplants of kidney may survive much longer periods in the human being than in the dog.

It is quite improbable that human livers could be transplanted with survival of the transplants, not so much because of the technical difficulties but more so because of the difficulty of obtaining a suitable donor liver. There is no question but that a temporary functioning liver transplant would have a place in the treatment of patients with chronic liver disease and especially those in acute failure or coma. In the latter condition recovery of the liver is possible in many instances and a temporarily functioning transplant would tide the patient over. It is our present interest to determine how effective liver transplants can be in animals with hepatic failure and deficiency states. Short of actual transplantation of the liver is the technique of viviperfusion using animals in liver failure and donor livers. This technique is being investigated currently in our laboratory. The subject of heterotransplants in the case of the liver is also of interest in that short-term function of donor livers would have value.

The peculiar bacterial flora of the dog's liver[10] and its uncertain and difficult eradication[11] caused a significant number of failures in the group prepared with antibiotics, since there was no way to predetermine the efficacy of our preparation. This factor was controlled in the present experiment by reducing the period of complete hepatic anoxia to a few minutes, through the use of an arterial shunt. Since the human liver is usually sterile, we believe that it is of importance to investigate the reactions which occur after transplantation of normally sterile livers in other species. We have transplanted livers in monkeys *(Macacus rhesus)* but, so far, the technical difficulties have not been overcome and we have had no survivals.

Another difficulty encountered in this study in which dogs have been used, namely, central lobular congestion, may be due to the activity of the hepatic vein sphincters.[12]

At the present writing we have very little data on the composition of the bile excreted by the liver transplants. The active formation and excretion of bile is incontrovertible and the gross appearance and texture of this bile is quite normal. We have noted that during periods of greatest transplant activity, as indicated by Bromsulphalein retention curves, definite blue discoloration of the bile occurred for one to two hours after injection of the dye.

Liver transplants may prove useful in the study of hepatic physiology. Although technically difficult and time-consuming, the procedure may also provide a useful technique for investigations in such varied fields as shock, homeostasis, immunity, and hormone metabolism.

SUMMARY AND CONCLUSIONS

A description of several techniques used for the transplantation of the liver in dogs has been given, together with observations on forty-nine experiments.

The entire liver of the dog can be transplanted intact to another dog with preservation of function in so far as the excretion of bile is concerned for periods up to five days.

The liver seems to be subject to the same type of homotransplantation reaction as is the kidney when transplanted in the dog. Microscopically, the changes

first seen in the liver are small round cell and mononuclear infiltration of the periportal spaces which occur about the fourth day. Thereafter, necrosis begins and progresses rapidly, being complete usually by the end of the fifth day.

Bile production and Bromsulphalein extraction are maximum on the third day after transplantation of the liver.

None of the canine livers in this experiment tolerated complete anoxia for a period over thirty-three minutes, in spite of preparation with antibiotics.

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CANCER OF THE THYROID GLAND

Clinical Analysis and Evaluation of Therapy in 144 Patients

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(From the Samuel D. Gross Surgical Division of the Jefferson Medical Center)

DESPITE increasing interest in cancer of the thyroid gland, refinements in clinical and pathologic diagnosis, and improved surgical and radiologic therapy, the management of the individual patient still remains controversial. A single surgeon tends to gain impressions from his isolated cases, whereas a true knowledge of this disease requires the accumulation of data from group experience. It is our purpose to review such experience at the Jefferson Medical Center during the past thirty years and particularly to evaluate the results of therapy.

CLINICAL EVALUATION

Incidence.—Between the years 1923[1] and 1954, 3,644 patients with disease of the thyroid gland were encountered in the surgical division of Jefferson Hospital. There were 144 patients with thyroid cancer, an average incidence of 4.0 per cent. The increase in incidence during the past three decades from 2.2 per cent to 6.8 per cent is shown in Fig. 1. This reflects the increase in surgery for nodular nontoxic goiter in which most thyroid cancer is found and the decrease in surgery for diffuse toxic goiter since the advent of antithyroid drugs. Thus, in our previous analysis of 200 surgical goiter cases in the years 1948 to 1951[2] at Jefferson Hospital, only 6 per cent were operated upon for diffuse toxic goiter and more than twice this percentage had cancer of the gland.

Fig. 2 demonstrates that the peak incidence of thyroid cancer (65 per cent) occurred between the fourth and seventh decades, and 13 per cent occurred within the first three decades. Women predominated in a ratio of 2.3 to 1, but in the fifth and sixth decades the incidence in men almost equaled that in females.

Symptoms and Signs.—Any nodule in the thyroid gland can be cancer, and none of the additional symptoms and signs listed in Table I should be awaited in order to arouse suspicion of this lesion. The preponderance of cancer in single nodules (66 per cent in this series) has been amply established in previous reports of others.[8, 9]

Size of the Lesion.—About one-half the cancers were 1.5 cm. in diameter or less. One-third were between 2 and 4 cm., and the remaining one-sixth were over 4 cm. in diameter.

Type of Cancer.—Table II lists the histologic types of cancer of the thyroid gland encountered in this series. Although papillary carcinoma composed

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only 40 per cent of the thyroid cancers in the series, during the last five years it was found in 61 per cent of the patients. This is explained by the fact that during recent years, our pathology department[7] has been diagnosing almost all papillary lesions of the thyroid gland as malignant.

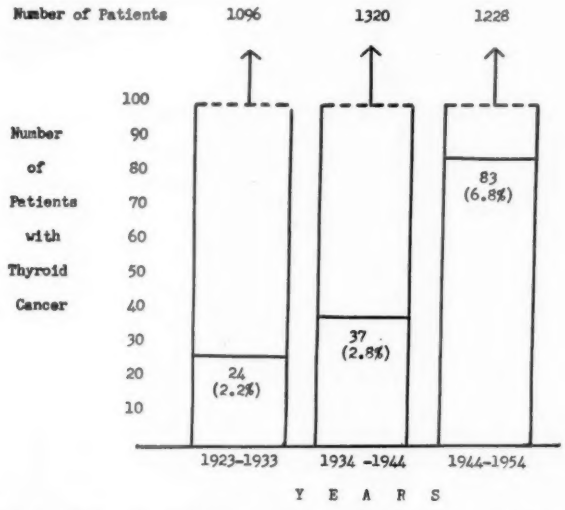

Fig. 1.—Incidence of thyroid cancer during three successive decades among 3,664 patients with thyroid disease.

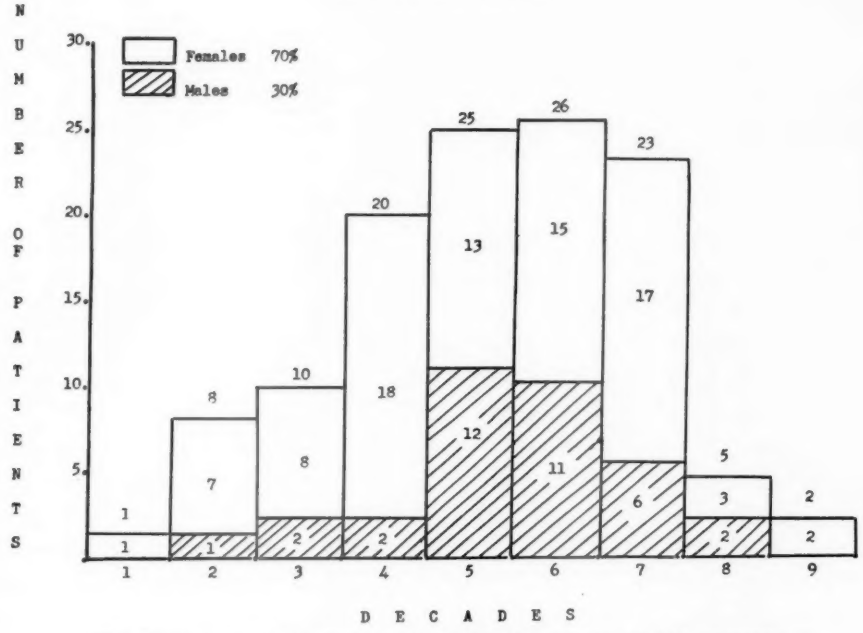

Fig. 2.—Age and sex incidence of thyroid cancer of 144 patients.

Delay in Treatment.—Only 18 per cent of the patients in this series underwent treatment within three months of the known onset of their goiter. About 40 per cent of the patients delayed at least one year. Twenty-three per cent of the patients were known to have a mass in the thyroid gland for five years or more. In this latter group, it is possible that in some of the patients an adenoma underwent malignant change.

TABLE I. THE MORE COMMON SYMPTOMS AND SIGNS IN THYROID CANCER (120 Patients,* 1934 to 1954)

SYMPTOMS	NO.	PER CENT	SIGNS	NO.	PER CENT
Swelling in the neck	98	81.7	Mass palpable in the neck	118	98.4
Recent growth of swelling	25	20.8	A single nodule in the thyroid gland	79	65.9
Any type of discomfort in the neck	73	60.8	Multinodular thyroid gland	31	25.7
Weight loss	22	18.3	1) one lobe	14	11.6
Some voice change	16	13.3	2) both lobes	17	14.1
Persistent hoarseness	5	4.2	Palpable cervical lymph nodes†	16	13.3
			Palpable cervical nodes only	8	6.8
			Nothing palpable in the neck‡	2	1.6

Only one patient in this series had unequivocal evidence of hyperthyroidism. There were several in whom there was a question of borderline toxicity.

*The signs and symptoms of the 24 patients seen between 1923 and 1933 were not available.

†Twenty-seven patients were found to have lymph node metastasis at the time of surgery.

‡These patients had only hoarseness and dysphagia, respectively. The diagnosis was proved by tracheal and esophageal biopsy.

TABLE II. HISTOLOGIC TYPE OF TUMOR* IN 129† OF THE PATIENTS WITH THYROID CANCER (1923-1954)

TYPE OF CANCER	NUMBER OF PATIENTS	PER CENT OF PATIENTS
Papillary	51	39.6
Adenocarcinoma	58	45.0
Diffuse carcinoma	9	6.8
Giant cell	3	2.3
Hurthle cell	5	3.9
Epidermoid	1	0.8
Sarcoma	2	1.6

*Classified after Herbut.[6, 7]

†Nine patients in the first decade of the series and six in the succeeding two were treated without histologic proof of the diagnosis.

TREATMENT

Table III lists the operative procedures performed on 116 of the 120 patients treated between 1934 and 1954. Information on the exact surgical procedures performed between 1923 and 1933 was not available. It is evident that numerous procedures were used, based upon the histologic type and extent of the cancer, as well as the individual concepts of the surgeons who participated in this series.

Fifty-seven of these patients received x-ray therapy in conjunction with surgery, or as the only therapeutic measure. Our criteria for x-ray therapy in cancer of the thyroid gland are: (1) patients in whom the surgeon or pathologist feels the cancer was not adequately removed; (2) patients who have inoperable lesions; and (3) patients with metastatic lesions causing symptoms.[3] Radioactive iodine was used in four patients to destroy any remaining thyroid gland not removed surgically or to inhibit metastatic lesions which took up at least 1.5 to 2 times the amount of radioactive iodine as did the bone marrow.

FOLLOW-UP

Eighty-five patients of 101 who were eligible were followed for five years, or 84 per cent. The status of these patients is shown in Table IV. It will

TABLE III. SURGERY PERFORMED ON 116 OF THE 120 PATIENTS* SEEN BETWEEN 1934 AND 1954

PREVIOUS SURGERY (PERFORMED ELSEWHERE)		FIRST OPERATION AT JEFFERSON HOSPITAL†		SUBSEQUENT SURGERY AT JEFFERSON HOSPITAL	
OPERATION	NUMBER PERFORMED	OPERATION	NUMBER PERFORMED	OPERATION	NUMBER PERFORMED
None		Total thyroidectomy and radical neck dissection	5	None	
None		Total thyroidectomy and laryngectomy	1	None	
Subtotal thyroidectomy	1	Total thyroidectomy	10	Tracheotomy	2
Subtotal lobectomy	1	Total lobectomy and radical neck dissection	9	Tracheotomy	1
Subtotal lobectomy	2	Total lobectomy	19	Radical neck dissection	2
None		Total lobectomy and subtotal lobectomy	7	Tracheotomy	1
None		Subtotal thyroidectomy	21	Total thyroidectomy	1
				Total thyroidectomy with radical neck dissection	1
None		Subtotal lobectomy	24	Tracheotomy	2
				Radical neck dissection	2
None		Excision of nodule	6	Total thyroidectomy	1
Total lobectomy	2	Incisional biopsy	12	Tracheotomy	1
Subtotal thyroidectomy	2				
None		Tracheotomy only	2	None	

*Information on the exact surgical procedures performed between 1923 and 1933 was not available.

†Tracheotomy was performed as an adjunct to a definitive surgical procedure in 10 of these patients. Thirty of these patients also had lymph node biopsies.

TABLE IV. STATUS OF 85 PATIENTS AT THE TIME OF THE FIVE-YEAR FOLLOW-UP (85 PATIENTS WERE FOLLOWED OF THE 101 WHO WERE ELIGIBLE, OR 84 PER CENT)

	NO. OF PATIENTS	APPROXIMATE PER CENT OF PATIENTS
I. Alive	34	40
A. Without evidence of of recurrence	27	32
B. With recurrence	7	8
II. Dead	51	60
A. Died of cancer	48	57
B. Died of other causes	3	3

Thirty-two of the 34 five-year survivors had their lesion removed surgically. The other 2 had x-ray therapy only.

be noted that 60 per cent of the patients were dead and only 32 per cent were alive without clinical evidence of recurrence or metastasis. Fig. 3 compares the five-year survival rates in the patients receiving palliative treatment with those who underwent excision of the cancer. As would be expected, only 2 of 29 patients receiving palliative treatment (7 per cent) survived five years, while 32 of 56 patients (57 per cent) having surgical removal of the cancer survived. Lest the latter figure create undue optimism, it was found that only 7 of 41 patients followed ten years (17 per cent) were alive. Twenty-nine patients were followed fifteen years and 4 of these (14 per cent) survived.

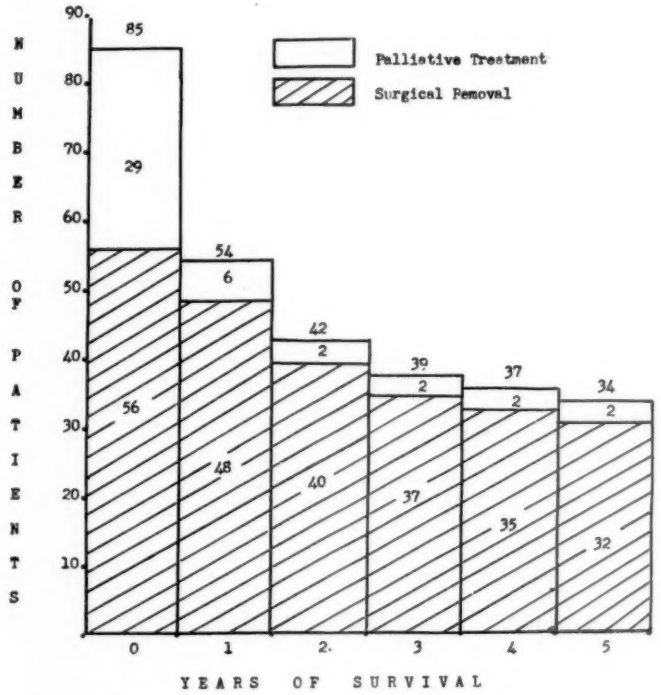

Fig. 3.—Five-year survival following treatment for thyroid cancer (85 patients followed five years). Palliative treatment consisted of surgical decompression, tracheotomy, or irradiation, or a combination of these.

DISCUSSION

It is evident from the clinical and follow-up data in this series that cancer of the thyroid gland is a ruthless killer, like cancer elsewhere in the body.

The anaplastic forms are rapidly fatal, and the low-grade papillary types produce death as an end result, only perhaps in a more subtile and prolonged process. It is our belief that undue emphasis[10] has been placed upon histologic typing and grading as a guide to the surgical treatment. It is necessary to know that the lesion is cancer at the initial operative procedure in order to carry out adequate surgical therapy, but we feel that knowledge of the type should not modify the actual procedure which we advocate as total thyroidectomy.

All too often in this series, frozen section was not performed, and the information that the lesion was actually cancer came as a surprise when the routine histologic report was received days later. In such instances the surgeon was reluctant to propose further surgery and tried to ease his mind by passing the problem on to the radiologist. Frozen-section study of thyroid nodules must be made if the surgeon is to carry out so radical a procedure as total thyroidectomy, for we do not believe this operation to be justified without a positive diagnosis. Unfortunately, with present frozen-section techniques, the pathologist is reluctant to give a positive diagnosis of cancer in about half the cases. When the lesion is an outright cancer there is little difficulty. On the other hand, when the cancer is low grade and must be differentiated from a benign adenoma, the pathologic diagnosis may be difficult even on routine paraffin section. In such instances, with minor distortions of the tissue on frozen section, as well as the fewer sections studied, the pathologist may hesitate to give a final diagnosis.[7] We do not feel that these difficulties should dissuade the surgeon from requesting this aid. In those instances in which the frozen section is equivocal, we advocate total lobectomy with removal of the isthmus at the time, and subsequent total thyroidectomy if the final report is malignant. This additional safeguard is warranted if one is dedicated to attempts at improving the survival rates of this disease.

We advocate total thyroidectomy as the initial operative procedure, whenever feasible, for the following reasons: (1) the thyroid gland is morphologically a single organ with rich anastamosis of the blood and lymph vessels of both lobes; (2) in our own experience, and in the reports of others,[4, 5, 10] multiple foci of thyroid cancer have been found in both lobes, either as multicentric foci of origin or contralateral metastasis; (3) the operative procedure of total thyroidectomy is not formidable, and, in most instances, with proper precautions, the parathyroid glands and the recurrent laryngeal nerves can be preserved; also, adequate replacement therapy for the hypothyroidism is readily available if necessary; (5) if the prognosis of thyroid cancer is to be improved, a more radical approach than that generally carried out in this series appears to be necessary.

Whether the incidence of regional lymph node metastasis is high enough to warrant routine radical neck dissection as part of the initial surgical procedure for thyroid cancer has not been settled. Martin[11] believed that it is, but the majority of surgeons prefer gross evidence of lymph node metastasis as the indication for this procedure. Opinions as to how the nodal metastasis

should be attacked vary from simple excision of individually enlarged nodes[12] to radical neck dissections, in some instances even bilateral[11] or combined with transsternal anterior mediastinal node dissection.[13]

We perform radical neck dissection when there is positive evidence of metastatic cancer to lymph nodes by frozen-section examination or gross evidence of tumor invasion of the veins. Nodal metastasis is looked for at the original total thyroidectomy, and, if found, a radical neck dissection is performed on the involved side at the time. If enlarged cervical nodes develop during the follow-up period, biopsy is performed and, if positive for cancer, a radical neck dissection is carried out. This procedure in our hands consists of the en bloc removal of the strap muscles, sternocleidomastoid muscle, jugular vein from the base of the skull to level of the clavicle, and the cervical nodes. The spinal accessory nerve is sacrificed whenever there appears a possibility that it may be involved or may hamper the extent of the dissection. The submaxillary gland is removed only when involvement of its triangle seems likely.

SUMMARY AND CONCLUSIONS

1. Of 3,644 patients with thyroid disorders on the surgical service of Jefferson Hospital, there were 144 patients, or 4.0 per cent, who had cancer of this gland. The incidence of thyroid cancer predominated between the fourth and seventh decades (65 per cent), with the ratio favoring women 2.3 to one.

2. Sixty-six per cent of the thyroid cancers in this series occurred in single nodules. About one-half the cancers were 1.5 cm. in diameter or less. The majority were of the papillary type (61 per cent during the past five years).

3. Only 18 per cent of the patients underwent treatment within three months of the known onset of their goiter. This emphasizes the regrettable delay that occurs in the vast majority of cases. Any thyroid nodule can be cancer and should be subjected to frozen-section study.

4. The varying operative procedures listed in Table III were generally conservative. We now feel that the only adequate surgical therapy for any type of thyroid cancer is total thyroidectomy. Radical neck dissection on the involved side is recommended at the time of initial surgery if there is evidence of spread to the adjacent lymph nodes or veins.

5. The over-all survival of the eighty-five patients followed five years was 40 per cent. Of 56 patients followed who had the thyroid cancer removed, 57 per cent survived five years. We feel that this prognosis could be improved by prompt surgical treatment of thyroid nodules, frozen section study at operation, and total thyroidectomy for cancer.

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A SIMPLE SURGICAL APPLIANCE FOR PECTUS EXCAVATUM*

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THE operative correction for pectus excavatum has been performed for a sufficient length of time to be adequately evaluated. Although variations of technique have been described, it is now generally agreed that the more radical procedures offer the best hope for long-term good results. Following such repair some method of sternal fixation must be employed until the sternum is stable.

Probably the oldest method for maintaining the sternum in position was the application of traction by means of a fracture bed. This was generally inconvenient, particularly in young patients. Traction applied to casts, jackets, and splints made of wood, plastic, or metal placed across the chest has been employed with good results. Fixation of the sternum without the use of external appliance has also been performed successfully by means of several periosteal sutures across the transverse wedge osteotomy with or without additional support from the adjacent soft tissues, costal cartilages, or a free rib strut.

The degree of paradoxical motion noted immediately postoperatively is usually marked. It therefore seems than any method of internal fixation requires a bony brace of some sort to guarantee true stability. This implies extension of an already radical procedure. Moreover, internal fixation does not permit postoperative adjustment of the position of the sternum if this becomes necessary. The external splints in common usage can be adjusted by detaching and reapplying steel wires or silk strands and reattaching them at a different level. However, this would be very inconvenient in the event that postoperative roentgenograms indicated a change of position.

A chest splint was devised which is thought to have the advantages of simplicity, stability, and variability. The essential features consist of a stainless steel bar slightly rounded to conform to the contour of the chest and of sufficient length to suit the individual case. (Three sizes were thought to be adequate.) This is bolted to hard rubber blocks at either end, which are applied against the chest. Although sponge rubber has been used in addition, it has been found to be unnecessary. A square opening is centrally cut, through which a length of square-threaded stainless steel slides freely, but not enough to allow rotation within the opening. Heavy braided silk passed through the sternum is then looped through holes at one end of this

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*Manufactured by E. Miltenberg, Inc., New York 12, N. Y.

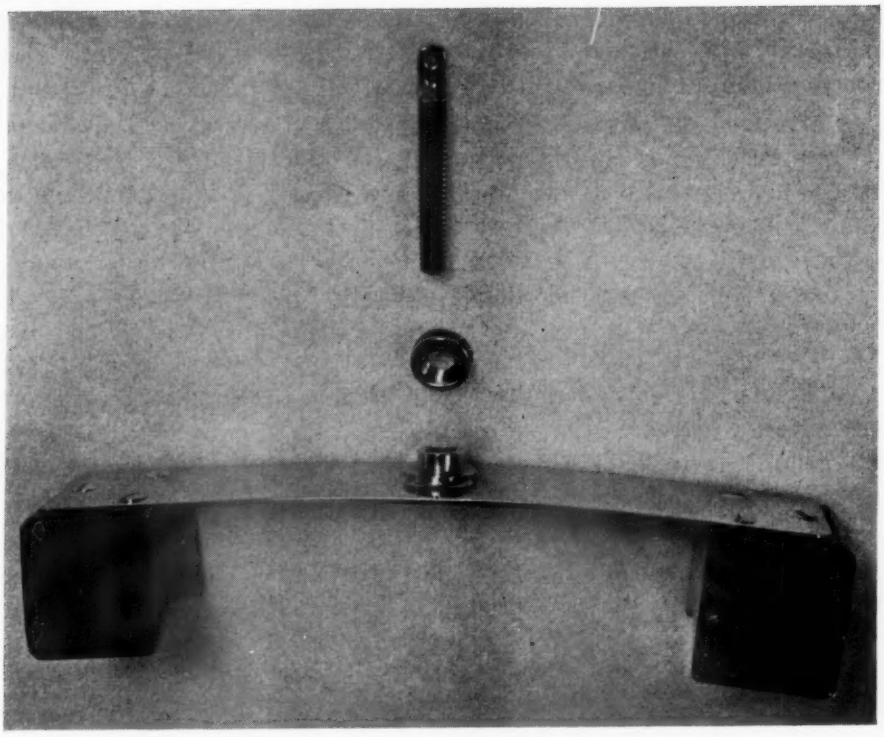

Fig. 1.—Essential parts of chest splint (see text).

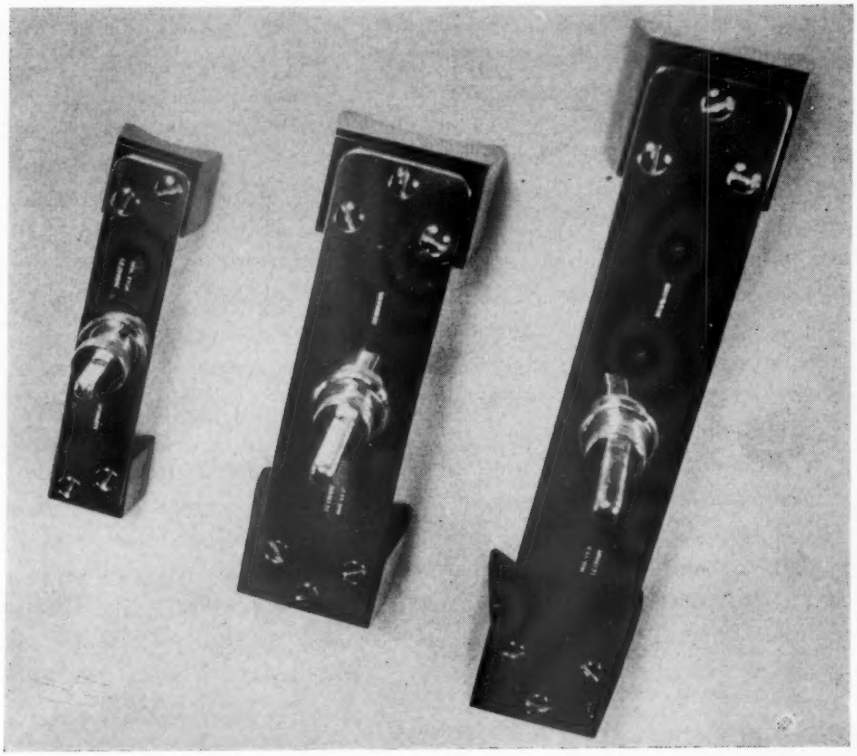

Fig. 2.—Set of assembled chest splints; 4, 5, and 7 inch lengths comprise set.

and tied. At the other end a knurled nut is threaded and turned until the sternum reaches a satisfactory position. Turning clockwise will result in elevation and counterclockwise in depression of the sternum (Figs. 1 and 2).

This arrangement obviates the necessity for a swivel at the sternal end which might stick and cause twisting of the silk strands. Necessary postoperative adjustments are then made by simply turning the nut in the desired direction. Since the splint is elevated from the chest by the hard rubber blocks, the wound can easily be treated beneath the splint under good vision without disturbing the traction device.

CONCLUSIONS

1. Adequate fixation of some type is necessary for maintaining the sternum in position following correction of pectus excavatum.

2. A simple device is described which is easily sterilized, easily constructed, compact, and reusable.

3. The amount of traction can be varied very simply at any time.

4. The wounds can be inspected or treated quite easily without disturbing the splint.

TRACHEOSTOMY

Technique for the Creation of a Permanent Tracheal Opening

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THE surgeon is sometimes confronted with the necessity of performing a tracheostomy in a patient with an incorrectable permanent obstruction of the upper airways. The interference with breathing can be the consequence of pathologic conditions, such as in advanced Paget's disease of the facial bones, scleroma of the larynx, and so on. Or the stenosis of the airway may have been produced by a scarring process after extensive surgery on the larynx, pharynx, or traumatic injuries of these structures. In inoperable cases of cancer of the larynx, tracheostomy is one of the palliative measures to be used.

When the obstruction of the airway is a permanent one, the tracheostomy opening has to remain permanently to secure respiration. Some problems then arise. 1. After leaving the hospital, the patient or his relatives have to clean the tracheostomy tube. Often it is difficult for them to reinsert it into the trachea. The patient cannot remain without the tube for long periods of time because he may have serious difficulty in breathing. 2. It is more comfortable for the patient if the tracheostomy is of a lower type. In cases of inoperable cancer of the larynx the palliative tracheostomy has to be placed very low to avoid the invasion of the tracheal opening by the tumor. Sometimes it actually has to be a "retrosternal tracheostomy," the opening of the tracheal wall being placed in the upper mediastinum. This increases the difficulty for the patient or his relatives in inserting the tube, more so when the patient has a short neck. 3. The continuous pressure of the convexity of the tracheostomy tube on the upper rim of the tracheal opening provokes abrasion of the tracheal cartilages, with consequent progressive ascension of the tube. This is particularly marked in the lower type of tracheostomy. 4. In cases of palliative tracheostomy for inoperable cancer of the larynx, the progressive infiltration of the neck by the tumor will distort the relative positions of the opening on the skin and the one on the tracheal wall. The trachea will be placed deeper and deeper in the neck and in the mediastinum, and the use of a longer tracheostomy tube is then necessary.

From all this it is evident that the ideal palliative tracheostomy should fulfill the following requisites: It should be of a lower type and, if the case requires it, the tracheal opening should be placed in the upper mediastinum. Both the skin and tracheal openings should be large enough and built in such a way as to allow the patient to remain without the tracheostomy tube for long periods of time with no danger of obstruction due to the retraction of the tissues. The insertion of the cannula into the trachea should be a very easy maneuver for the patient. The operation should produce a fixation of the trachea upward

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and forward (tracheopexia). And the procedure should be carried out in such a way as to facilitate the rapid epidermization of the tunnel connecting the skin opening with the tracheal opening.

In an attempt to solve the problems created by a palliative tracheostomy, we have evolved a technique of tracheostomy with the use of a skin flap.[1] In the first patient operated upon, we made a presternal skin flap in the shape of an inverted U, which was sutured to the inferior rim of the tracheal opening. However, this flap was too small (it was only 3 cm. long) and it was sutured to the trachea under too much tension. On the seventh day after the operation the suture broke down completely. We then modified the procedure, making a longer and wider skin flap, with good blood supply, and undermining the skin of its base in order to facilitate an adequate advancement and sliding of the flap. It was possible then to suture the skin flap to the trachea without much tension, and the healing of the wound was satisfactory.

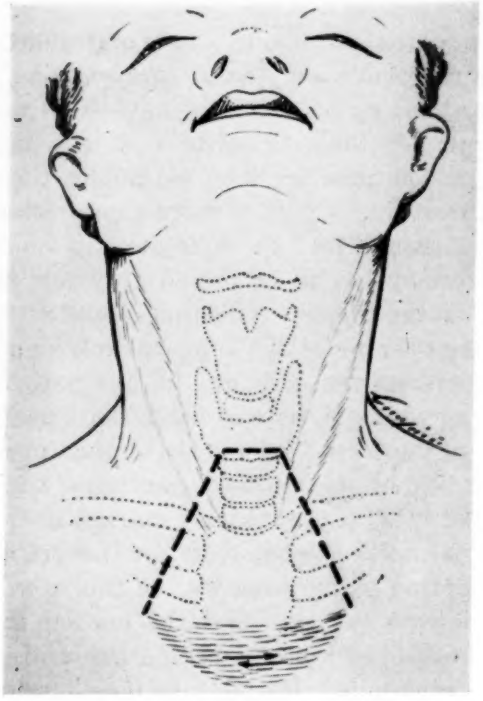

Fig. 1.

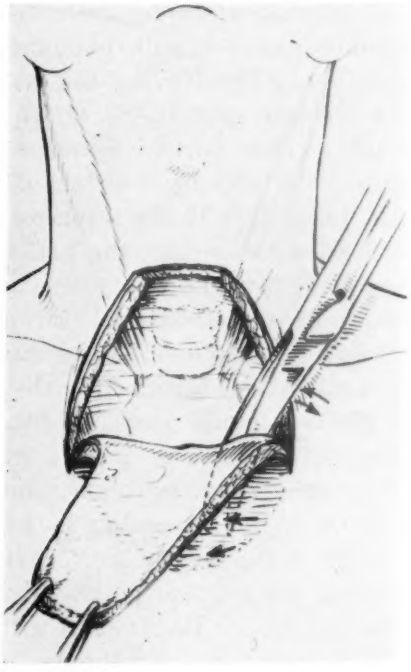

Fig. 2.

Fig. 1.—Presternal skin flap; undermining of the skin of its base.
Fig. 2.—Undermining of the skin to permit the advancement of the flap.

TECHNIQUE OF THE OPERATION

As in any tracheostomy, this procedure can be performed either with local or general anesthesia, according to which is more convenient in each particular case.

The skin flap has the shape of an inverted U (Fig. 1). The first incision is horizontal, 2.5 to 3 cm. long, placed halfway between the cricoid cartilage and the sternal notch. The lateral incisions begin at the extremities of the horizontal incision and continue obliquely downward and outward for about 10 cm. If the skin has been heavily irradiated and there is the possibility that the flap could undergo slough, then it would be convenient to delay the flap. However, this possibility is infrequent.

The skin flap is elevated including the subcutaneous adipose tissue and some inconstant fibers of the platysma muscle. The manubrium, covered by the pectoral fascia, is exposed, as well as part of the clavicles, pectoral regions, and the sternomastoid muscles at its insertion on the sternum. The skin at the base of the flap is undermined (Fig. 2). The extent of the undermining is regulated by the amount of advancement necessary to attach the skin flap to the trachea under moderate tension.

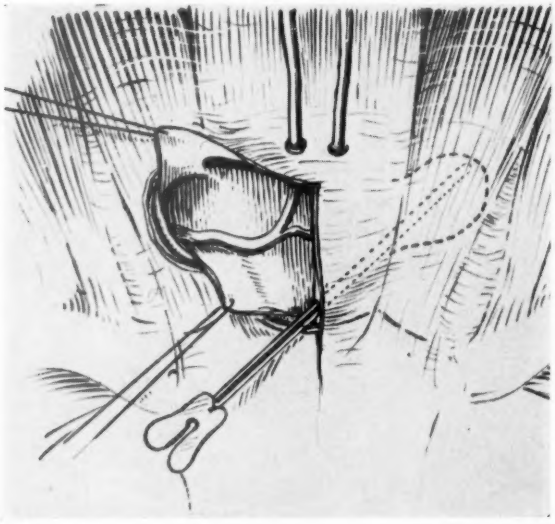

Fig. 3.—Suprasternal space. On the right side the superficial sheet of the investing layer of cervical fascia and part of the sternomastoid muscle have been elevated to show the lateral cul-de-sac of Gruber traversed by the anterior jugular vein. The two anterior jugular veins are connected by its transverse branch (partially imitated from Testut).

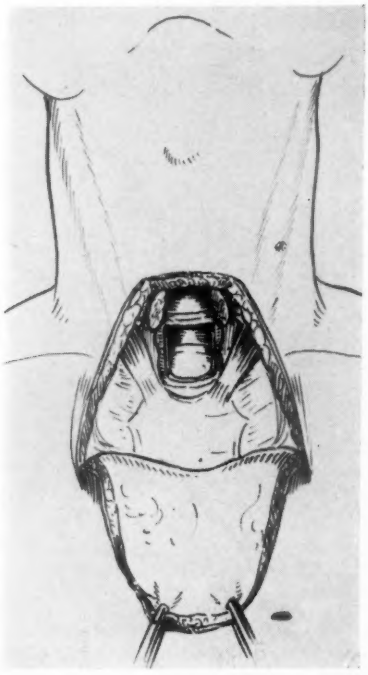

Fig. 4.—The isthmus of the thyroid gland has been sectioned in the midline. A square window including two tracheal rings has been made on the tracheal wall.

Between the sternal origins of the sternomastoid muscles and the sternal notch, the suprasternal space (space of Burns) is demarked by the two sheets of the investing layer of cervical fascia. The outer lamina is attached to the anterior border of the manubrium and the inner lamina to the posterior border and the interclavicular ligament.[2] The inner lamina is reinforced by the middle cervical fascia. .There are two lateral extensions of this

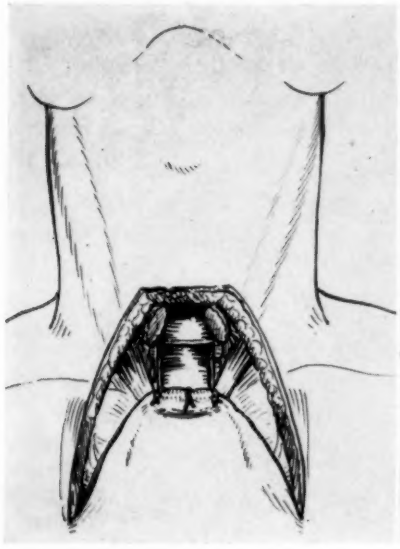

Fig. 5.

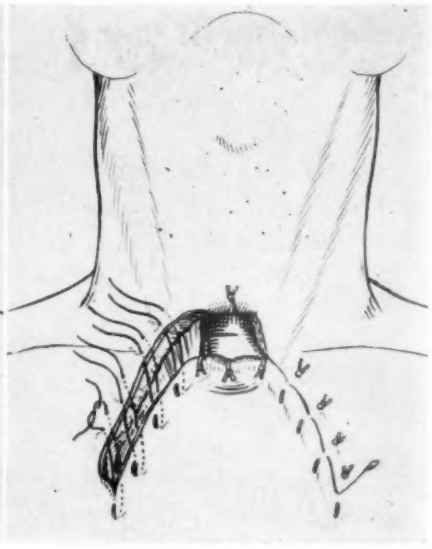

Fig. 6.

Fig. 5.—The skin flap is sutured to the lower rim of the tracheal window.
Fig. 6.—The lateral incisions are sutured.

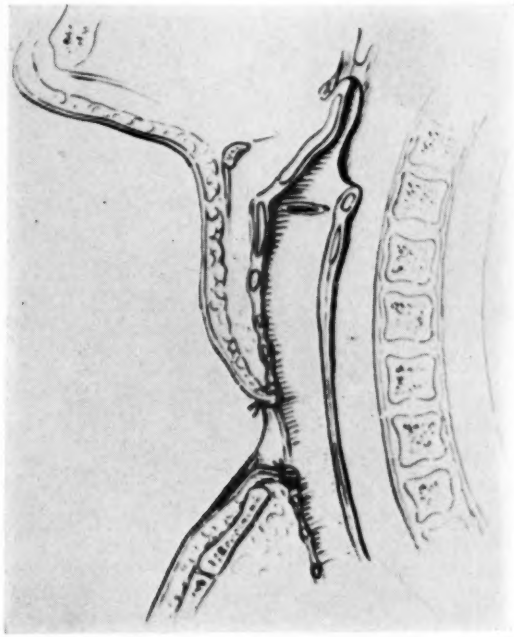

Fig. 7.—Sagittal section showing the skin flap invaginated into the depth of the neck, sutured to the trachea. It produces a fixation of the trachea forward and upward. It lines the lower part of the tunnel created between the skin and the trachea, thus favoring its rapid epidermization.

space which is prolonged laterally behind the heads of the sternomastoid muscles (cul-de-sac of Gruber). The space is filled with adipose tissue and a few inconstant lymph nodes. It is traversed by the two anterior jugular veins and its transverse connecting branch (Fig. 3).

The fascial and adipose tissues of the suprasternal space are removed and the vessels tied. The infrahyoid muscles then appear. They can easily be displaced laterally. The thyroid gland is displaced upward, or its isthmus sectioned in the midline. If the gland is in the way, a median portion of it should be removed. The trachea appears clearly, covered by the thin pretrachheal fascia (a prolongation of the visceral fascia of the mediastinum) with its previsceral fascial cleft. The latter permits the trachea its characteristic normal mobility. It also offers an excellent cleavage for blunt dissection, which can be carried as low into the mediastinum as needed. The elevation of the skin flap gives an ample exposure of this area. At the desired level, a square window including two tracheal rings is made on the tracheal wall (Fig. 4).

Fig. 8.—Patient operated upon with the technique described. The threads of the stitches uniting the skin flap to the trachea can be left uncut to facilitate its removal.

The hemostasis is completed and the suture of the skin flap is carried out. In case the flap had not been entirely mobilized, the undermining of the skin at its base is completed. In order to decrease the secondary retraction of the flap, which might cause a breakdown of the suture, it is advisable to fix the flap to the pectoral fascia which covers the sternum. A few stitches are made using the following technique: a needle threaded with absorbable surgical suture is inserted to take a bite of the fascia, and then passed through the undersurface of the flap at a point lying inferior to the fascial bite, so that when the suture is tied it will draw the mobile skin upward. This also eliminates a dead space. The tension effected upon the skin flap should be moderate; otherwise its blood supply could be impaired.

The skin flap is then sutured to the lower margin of the tracheal window with two of three stitches of nonabsorbable surgical suture (Fig. 5). The threads may be kept uncut and secured to the skin with cellophane tape to facilitate its removal. The skin flap has thus been invaginated toward the depth of the neck passing above the sternal notch. The two lateral skin incisions are then united with interrupted nonabsorbable surgical sutures (Fig. 6). Each suture is placed in such a way so that it lies obliquely across the line of incision, the bite of the skin flap being on a lower level than that in the opposite wound margin, so that when tied the flap will be drawn upward. This produces a moderate tension on the skin flap, thus helping its fixation. When suturing the upper extremity of these lateral in-

cisions it is necessary to avoid producing any narrowing of the airway. At the lower extremity of these incisions there will be an excess of skin on the external margin produced by the advancement of the skin flap. Buckling is overcome by the removal of two triangular sections of the skin or by a suture done as illustrated in Fig. 6.

A single stitch is made to bring the skin of the upper margin of the horizontal incision in contact with the upper rim of the tracheal window, or with the raw surface of the pre-

Fig. 9.

Fig. 10.

Figs. 9 and 10.—Patients operated upon with the procedure described. The tracheostomy opening is large and the patient can remain without the tracheostomy tube for long periods of time without difficulty in breathing. The maneuver of reinserting the tube is very easy. The patient shown in Fig. 10 has an extensive slough of the skin on the right side of the neck produced by heavy radiotherapy.

tracheal tissues (Figs. 6 and 7). This stitch usually becomes loose during the next few days. We do not think it necessary to complicate this operation with the use of an upper flap which would be sutured to the upper margin of the tracheal opening. The use of a split skin graft does not seem to be a practical procedure either.

A large tracheostomy tube is inserted and the conventional dressing is applied.

The procedure we have described is a simple one and solves many of the problems that arise when a palliative tracheostomy has to be performed. The skin flap produces a fixation of the trachea forward and upward, forming a bed for the tracheostomy tube which can thus be inserted into the trachea very easily. The tube will not exert much pressure on the upper rim of the tracheal opening, and the possibility of tracheal cartilage abrasion is reduced to its minimum. Because of the presence of the flap in the lower part of the tunnel created between the skin and the trachea, the epidermization and healing of the wound are accomplished much faster than in the ordinary type of tracheostomy. This procedure offers the patient a tracheostomy which is more comfortable and easier for him to handle.

SUMMARY

The problems that arise when a palliative tracheostomy must be performed are described. It is pointed out that an ideal palliative tracheostomy should fulfill the following requisites: It should be of a lower type; both the skin and the tracheal openings should be large enough and built in such a way as to allow the patient to remain without the tracheostomy tube for long periods of time. The insertion of the tube into the trachea should be a very easy maneuver for the patient. The operation should produce a fixation of the trachea upward and forward. And, finally, this procedure should facilitate rapid epidermization of the tunnel connecting the skin opening with the tracheal opening.

A procedure of tracheostomy is described with the use of a presternal flap in the shape of an inverted U which is sutured to the lower rim of a square window created on the trachea. This operation solves many of the problems that arise when a palliative tracheostomy has been performed.

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MANAGEMENT OF PATIENTS WITH PHEOCHROMOCYTOMA, INCLUDING TWO CASE REPORTS

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THE establishment of the diagnosis of pheochromocytoma and the management of patients with such tumors has been very difficult in the recent past. Frequently it has not been possible to establish the diagnosis with any degree of certainty except by operation. When the diagnosis was made preoperatively, localization of the tumor to the right or left adrenal gland area was very uncertain. This uncertainty led some to suggest that when a pheochromocytoma was suspected an abdominal laparotomy be performed first; then, when diagnosis of an adrenal tumor was established and the site of the lesion determined, to close the abdominal incision and remove the tumor through a flank incision. The operative mortality has been high. When the diagnosis was made preoperatively, the operative mortality was 26 per cent and when the patient had an operation for another condition and a pheochromocytoma was unrecognized, the operative mortality is said to have been 50 per cent.[1] One such fatality has occurred in our hospital in the past few years. With the currently available methods of diagnosis, localization, and management, these tumors are encountered more frequently and the operative mortality appears to have been greatly reduced. Indeed, it seems not unrealistic to predict that the operative mortality for recognized tumors should be reduced to a few per cent or perhaps a fraction of 1 per cent.

SYMPTOMATOLOGY

The most extensive review of this subject is that of Graham.[2] Frankel, a German, first described the disease, while the elder Charles Mayo[3] performed the first successful removal of a pheochromocytoma of the adrenal gland in 1927. The most common symptoms in order of frequency are (1) headache, (2) palpitation, (3) vomiting, (4) sweating, (5) dyspnea, (6) weakness, and (7) pallor, the symptoms of epinephrine overdosage. However, headaches occur in only 55 per cent and pallor in only 16 per cent of these individuals.[2] The typical attack is associated with hypertension. During an attack the blood pressure increases in the cases reported have been as little as 20 mm. Hg and as high as 210 mm. Hg. Some individuals, however, have a sustained type of hypertension. It has been estimated that each year in the United States from 600 to 800 individuals with sustained hypertension die of the effects

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of pheochromocytomas. These individuals probably could have been completely cured of this disease had it been recognized and treated properly. Ten per cent of the patients have the typical findings of diabetes mellitus. A pheochromocytoma may emulate hyperthyroidism and may cause swelling of the thyroid, exophthalmus, increased basal metabolic rate, and the protein-bound iodine values may be increased. There may be a temporary response to antithyroid medication.[4]

ESTABLISHING THE DIAGNOSIS

Pharmacologic tests are the cornerstone of diagnosis. Histamine[5] is the agent of choice for the provocative test. It however, is not entirely specific, both false positive and false negative tests having been recorded. After base-line blood pressures are obtained at five-minute intervals for one-half hour, 0.5 c.c. of normal saline solution is injected intravenously. Usually there is a slight rise in the blood pressure in response to the intravenous injection. When the blood pressure returns to the base-line level, 0.025 mg. of histamine base in 0.5 c.c. of physiologic saline solution is injected intravenously. Blood pressure readings are taken at one-minute intervals for fifteen minutes. A rise of more than 50 mm. Hg systolic and 25 mm. Hg diastolic is considered indicative of a positive test. In normal individuals, a sudden slight drop in pressure is followed by a slight rise in pressure. The administration of 5 mg. of Regitine (phentolamine) in 1 c.c. of sterile water intravenously during the peak of the elevation of blood pressure will rapidly reduce the pressure toward the base-line pressures.

A similar dose of Regitine[6] will also produce a marked temporary fall in blood pressure in the individuals with the sustained type of hypertension. Every individual with sustained hypertension of more than a moderate degree should have a Regitine test performed for obvious reasons. Following determination of the base-line blood pressure level, 5 mg. of Regitine is injected intravenously in 1 c.c. of sterile saline solution. The blood pressure is determined at thirty-second intervals for three minutes and then at one-minute intervals for seven minutes. A fall of 35 mm. Hg of systolic pressure or 25 mm. Hg of diastolic pressure is considered positive. False positive and false negative responses have been recorded but they are rare. It should be remembered that sedatives or narcotics administered within twenty-four hours of the test will produce a false positive reaction.[7]

The patients with pheochromocytoma are usually resistant to ordinary doses of epinephrine. If no response in pulse or blood pressure is obtained following the subcutaneous administration of 0.5 c.c. of 1:1,000 Adrenalin, the dosage is increased by 0.5 c.c. increments until a response is obtained. Mayock and Rose[8] have reported that 2.5 c.c. was necessary to produce a rise in blood pressure in a patient whom they reported. A quantitative chromotographic tests for circulating epinephrine and norepinephrine in the blood has been reported by Manger and associates.[9] Von Euler[10] has reported a chromotographic method of determining increased amounts of epinephrine and norepinephrine excreted in the urine. We have not employed these methods but recognize their potential usefulness.

LOCALIZATION OF THE TUMOR

Pyelography or simply roentgen films of the abdomen may reveal displacement of the upper role of the kidney by a tumor mass. Direct perirenal air injection for the radiographic demonstration of a tumor of the adrenal gland is not used because of the rather frequent deaths due to air embolism. Presacral oxygen injection as described by Scarinci[11] in 1950, however, appears to be a relatively safe procedure. We have used it in some 20 individuals. We know of only one fatality following the use of this technique.[12] It should be pointed out that in this fatality, which occurred in another hospital, air, not oxygen was used for the injection. Oscultation of the chest revealed sounds suggesting air embolism; this diagnosis was confirmed at post-mortem examination.

The patient is prepared for presacral oxygen injection as one would prepare a patient for pyelographic study. With the patient in the knee-chest position, a No. 18 or No. 19 intravenous needle is inserted in the midline at a point equidistant from the anal orifice and the tip of the coccyx. The tip of the needle is advanced in the areolar tissue between the anterior surface of the coccyx and the posterior wall of the rectum. The position of the tip of the needle is determined by digital rectal examination. By means of a three-way stopcock and appropriate rubber tubing, a 50 c.c. syringe is filled with oxygen from an inflated rubber anesthesia rebreathing bag filled with oxygen. In ten to fifteen minutes, 1,000 to 1,400 c.c. of oxygen is injected with a 50 c.c. syringe in an adult. The total amount depends upon the relative size of the individual. As the injection progresses, the patient has a feeling of fullness similar to that experienced with the administration of an enema. There may be slight iliac fossal pain or more pronounced lumbago. If discomfort is present, usually it is decreased markedly within one-half hour, although phrenic pain which may develop after the injection may persist in a mild degree for twenty-four hours.

Immediately after the injection, the patient is placed supine on a tilting fluoroscopic table in the semierect position, 35 degrees head-up position. If sufficient oxygen is found on one side of the retroperitoneal area by fluoroscopic examination, the patient is placed for ten to fifteen minutes in the lateral decubitus position which will favor a more satisfactory gravity distribution of the oxygen. With an adequate amount of oxygen beneath the diaphragm and around the kidneys and adrenal glands, anteroposterior, lateral, oblique, and planographic views are taken. A pyelographic study can be made at the same time to provide double contrast.

OPERATIVE TREATMENT

There are three hazardous phases in the operative treatment of these patients.[13] The first is during the induction of anesthesia and positioning of the patient on the operating table. The second phase occurs when the tumor is palpated or manipulated by the surgeon. The third phase occurs immediately after removal of the tumor. Induction of anesthesia and positioning of the patient in the lateral decubitus position may excite a fatal attack of paroxysmal hypertension. The intramuscular administration of 5 mg. of Regitine before induction and repeated whenever the blood pressure becomes unduly elevated will prevent or abort a paroxysmal attack.

The anesthetists at the Hospital of the University of Pennsylvania believe that sodium thiopental should be used for induction followed by nitrous oxide maintenance of anesthesia through an endotracheal airway. Muscular relaxation is provided by an intravenous drip of succinyl choline. (The latter is a curareiform agent without a histamine-like action.) They are convinced that ether should not be used. In this respect they disagree with Apgar and Papper[1] who believe that maintenance of anesthesia should be by means of ether. Recent evidence indicates that part of the effect of ether anesthesia is due to a sympathetic nervous system stimulating action.[14] Because such an action should be avoided in patients with pheochromocytoma, ether should not be used.

The second hazardous phase occurs when the tumor is manipulated by the surgeon and large amounts of epinephrine and norepinephrine may be expressed into the circulatory system. Regitine can be used intravenously if the blood pressure becomes markedly elevated. Of course, the adrenal veins should be ligated as soon as possible to prevent continued dissemination of epinephrine and norepinephrine into the systemic circulation.

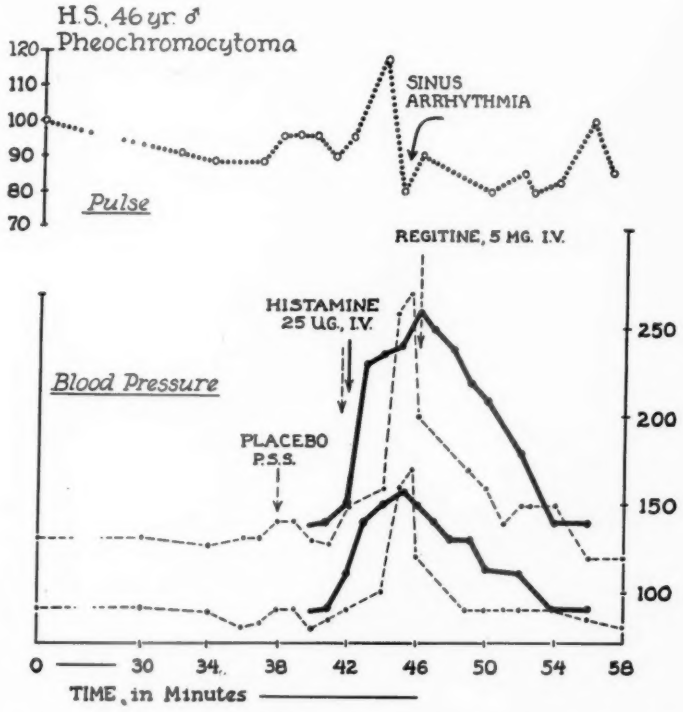

Fig. 1.—The heavy solid line shows a blood pressure response to 260 mg. of mercury systolic pressure following the injection of histamine. The blood pressure returned to approximately the base-line level in a period of about ten minutes. The broken lines show the blood pressure response in the same individual following histamine injection and then a marked depression of the elevated blood pressure toward normal following the administration of Regitine. The broken line represents changes in pulse rate following the injection of histamine.

The third hazardous phase occurs immediately after removal of the tumor when these patients are prone to develop shock. Shock may be due in part to the blood loss of operation, but it may also be due to the sudden withdrawal of a tumor which has been constantly providing the body with excessive amounts of epinephrine and norepinephrine. Shock is prevented by replacement of blood loss as it occurs during the operation and by the administration of norepinephrine or epinephrine by constant intravenous drip when hypotension appears. When removal of the tumor necessitates removal of one entire gland, replacement therapy in the form of adrenal extract, cortisone, desoxycorticosterone,

and so on, is not necessary. Adrenal medullary tumors do not depress adrenal cortical function and ordinarily the adrenal reserve is such that the remaining adrenal gland is more than capable of meeting the demands of the body.

CASE 1. The patient, H. S., was a 47-year-old white man who gave a history of attacks of palpitation, headache, pallor of the skin, and excessive perspiration followed by weakness of five years' duration. The blood pressure which was usually 120/80 was found to be 260/110 during one of these attacks. Physical examination revealed no abnormalities. Planograms, abdominal survey film, and urogram were negative. Laboratory tests were noncontributory. The glucose tolerance curve was normal. There was no response to ordinary doses of epinephrine administered subcutaneously or to the cold pressor test. Intravenous histamine produced a dramatic elevation of blood pressure and Regitine markedly reduced this abnormal elevation of blood pressure (Fig. 1). Presacral oxygen injection demonstrated a tumor of the left adrenal gland (Fig. 2). A pheochromocytoma,

Fig. 2.—In this oblique roentgen film of the abdomen following presacral oxygen injection, the pheochromocytoma was well demonstrated. The outlines of the kidney and the level of the right diaphragm were facilitated by the presence of the retroperitoneal oxygen.

confirmed by histologic diagnosis, was removed together with the remaining adrenal gland through a left subcostal incision. The twelfth rib was not resected. Regitine was used prophylactically during the operative procedure (Fig. 3). Five hundred cubic centimeters

of blood was administered during the operation. It was not necessary to administer epinephrine or norepinephrine to support the blood pressure following removal of the tumor. The patient has remained well for approximately three years postoperatively.

CASE 2. M. G., a 52-year-old white woman, complained of excessive perspiration of the trunk, arms, face, and neck of ten years' duration. She was unable to "work during the summer because of the heat." Two years earlier she had had a skin graft for an ulcer of the left heel. At that time she was told that she had a labile blood pressure, hyperglycemia, and glucosuria. During the past year she had had weakness and a weight loss of 15 pounds. There was excessive redness of the skin of the fingers and toes with occasional blanching of one or more of the digits. The basal metabolic rate determinations were plus 42 to plus 45 per cent. Because of a fasting blood sugar of 173 mg. per cent she was treated by a low carbahydrate diet and 15 units of protamine zinc insulin daily. She had never had clinical symptoms of hyperthyroidism or diabetes. Tachycardia with occasional premature contractions had been noted.

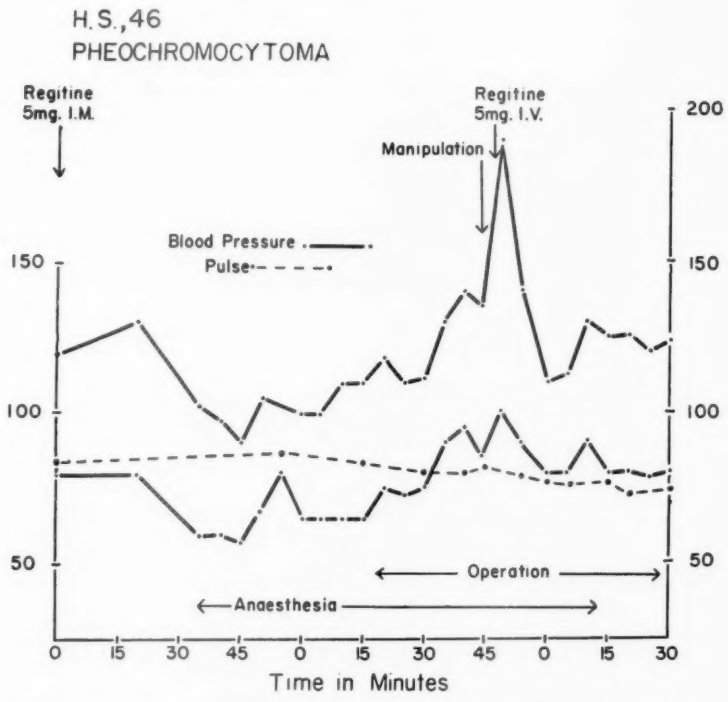

Fig. 3.—Blood pressure and pulse responses during anesthesia and operation for removal of a pheochromocytoma. Five milligrams of Regitine was injected intramuscularly prior to the induction of anesthesia and 5 mg. of Regitine was injected intravenously at the time of manipulation of the tumor.

A fundoscopic examination showed Grade II hypertensive retinopathy according to the classification of Keith, Wagner, and Barker. A Regitine test reduced the blood pressure from a base line of 218/122 to 164/82 in thirty seconds. Films taken following presacral oxygen injection failed to reveal an adrenal tumor. However, planograms were not taken at the time of the presacral oxygen injection. Planograms were taken on the day following and the films of this examination showed evidences of a right adrenal tumor. At operation on Nov. 22, 1953, a pheochromocytoma of the right adrenal gland was removed through a right subcostal incision with the patient in the left lateral decubitus position. The twelfth rib was not resected. The blood pressure became elevated at the time of manipulation of the tumor. The administration of 5 mg. of benediane* intravenously did

*Benzodioxane.

not reduce the blood pressure, but the blood pressure was reduced by the administration of Regitine. Five hundred cubic centimeters of blood was administered during the operation. A continuous drip of 4 mg. of norepinephrine in 1,000 c.c. of physiologic saline solution was necessary to maintain the blood pressure while the wound was being closed. The patient has remained symptom-free with normal blood pressure, basal metabolic rate, and fasting blood sugar, and she has gained 25 pounds during the four months following operation.

SUMMARY

A better understanding of the signs and symptoms of pheochromocytoma, the use of the Regitine test, histamine provocative test, epinephrine tolerance test, presacral oxygen injection technique preoperatively, and the use of Regitine, blood, and epinephrine or norepinephrine with avoidance of ether during operation will greatly facilitate the establishment of the diagnosis and the operative management of patients with pheochromocytoma. The management of these patients is illustrated by the case reports of two patients, one who had paroxysmal attacks of hypertension and one who had a persistent type of hypertension.

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LATERAL EPICONDYLITIS OF THE ELBOW TREATED BY FASCIOTOMY

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LATERAL epicondylitis is a painful syndrome of the elbow to which many pathologic conditions may be attributed. It is characterized by a dull, prolonged, recurrent aching pain in the region of the brachioradialis "mobile-wad" twist, deep and distal to the epicondyle. The pain can be aggravated by sudden wrist extensor tension, particularly with the arm extended beyond 160 degrees, or by repeated pronation-supination muscle action as in tennis or violin playing. The grip is weak when the arm is in certain attitudes. There is digital point-pressure tenderness over the lateral epicondyle of the humerus, particularly at the origin of the forearm extensors (extensors digiti propius, carpi ulnaris, carpi radialis brevis, digitorum brevis) and also the supinator.

The normal carrying angle of the elbow is approximately 165 degrees. The attachment of the tendinous and fascial bands of the extensor muscles, which originate at the humerus and insert through tendons along the forearm into the wrists and the digits of the hands, places the pressure-point tension cycle on the lateral condyle or, when the condyle of the humerus is prominent, along the lateral articular rim. With the forearm in pronation there is a loss of the carrying angle, with practically a straight-line formation from the shaft of the humerus on to the forearm. When the wrist is palmar-flexed or the hand gripped and in flexion, maximum tension is created along the extensor apparatus and on to the humerus. Full pronation of the forearm with dorsiflexion of the wrist and full flexion of the wrist with supination of the forearm usually are asymptomatic. When tension forces are created, as when the forearm is in full pronation and the wrist in extreme palmar flexion, the tension is exerted along the course of the extensor apparatus and this strikingly elicits the pain.

MECHANOPATHOGENESIS

Campbell[1] stated that the pathologic entity producing the lateral epicondylitis is a partial tear of the conjoined tendon, particularly at the site of extensor carpi radialis brevis muscle, or sometimes a tear between the tendinous origin of the muscle and the periosteum, with a subsequent traumatic

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bursitis and muscular contractures. He stated further that rarely it is an inflammation of the radial humeral bursa which lies between the conjoined tendon and the radiohumeral joint. Marlin,[2] in his report on the treatment of tennis elbow, stated that the partial tear of the conjoined tendon is converted into a complete tear, the tendon being detached from the chronically inflamed periosteum to which it adhered.

Conditions involving mechanical positions and repetitious motions, and trauma, making for a pathologic situation (Fig. 1) may be grouped as follows:

Group I: Occupational stress in which the elbow is maintained at full extension and the forearm in pronation while the hand performs repeated gripping motions, with replacement of the wrist and extreme flexion, continuously over the long periods of time and usually at high speed. A sudden jolt at the wrist joint while the hand is clenched will also produce symptoms; here, the initial strain is along the extensor fascia of the forearm and the clinical manifestations are usually in the hand or wrist, in which the patient feels a weakness (Fig. 1, *A*).

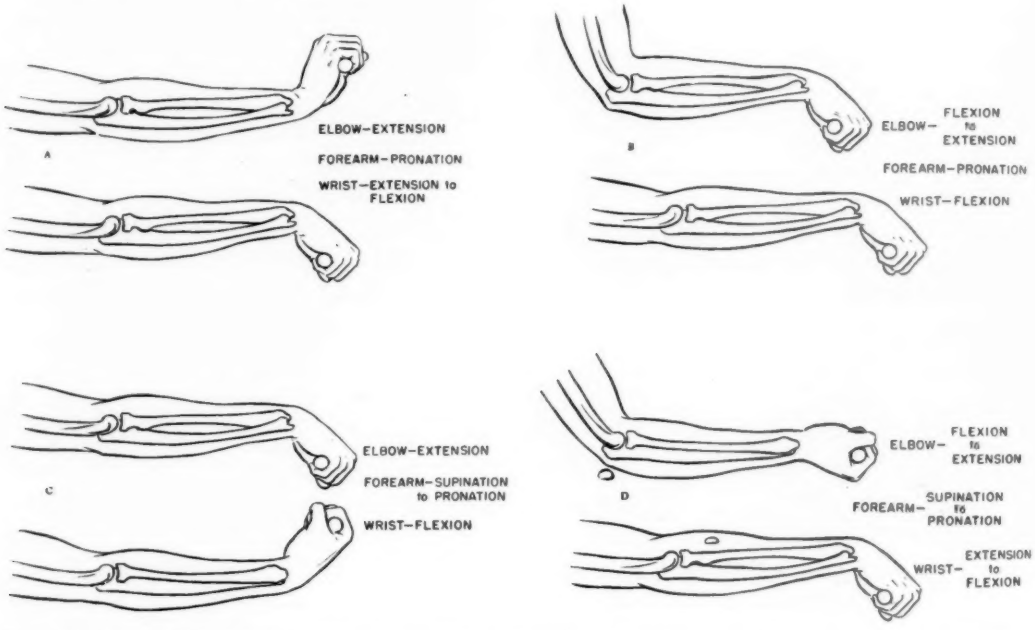


Fig. 1.—*A-D*, Mechanical positions denoting repetitious motions causing lateral epicondylitis.

Group II: Where the forearm is held in pronation with the hand gripping and the wrist in flexion (as in angling or strap-hanging) and a sudden powerful extension of the elbow occurs (Fig. 1, *B*).

Group III: Where the hand and wrist must be kept in a flexed gripping position, with the elbow in full extension, and a to-and-fro pronation and supination movement of the forearm is carried out. Constant repetition of this maneuver in occupation will excite symptoms of fascial tension in the region of the forearm (Fig. 1, *C*).

Group IV: Where the movements are conducted from one of complete fascial relaxation of flexion of the elbow, supination of the forearm, and extension of the wrist to a sudden jolt of simultaneous action of extension of the elbow, pronation of the forearm, and palmar flexion of the wrist with the digits clasped (Fig. 1, *D*).

Group V: Direct trauma against the lateral epicondyle.

Bursae are a common finding among industrial workers, such as machinists for instance, who are required to make continual to-and-fro motions from neutral to pronation of the forearm, a gripping with the hand, with flexion of the wrist and gradual extension of the elbow. Similar motions are carried out by plasterers, bricklayers, fishermen, airhammer and sawmill operators, and tennis players. An irritative bursitis may develop along a prominent condyle; or, if the lateral condyle is less prominent and the head of the radius is the projecting eminence, the bursa may occur at the latter site. In fact,

Fig. 2.—Maneuver of wrist movement inciting the symptoms of the lateral epicondylitis.

an adventitious bursa may be formed anywhere along the course of the radiohumeral joint wherever the tension is created. The violent flexion of the wrist with pronated forearm that occurs with tennis players and airhammer operators frequently precipitates a lateral epicondylitis of the elbow. It is still a question whether the entire syndrome is one of bursitis alone or if there is an associated tendinitis, fasciitis, neuritis, periostitis, or "regional myositis." If the elbow is maintained in a flexed position, little or no irritation of the lateral condyle can occur; however, in those movements requiring full extension of the elbow with pronation of the forearm and a gripping, clasping, or clenching of the hand, the origin of the extensor muscles is placed as a mechanical

purchase and tension is likely to lead to a development of epicondylitis. Perhaps the old theory of rupture and fraying, with fibrous thickening and fascial shortening of extensor connective tissues, is acceptable, particularly for diagnostic and therapeutic purposes.

We believe that loss of activity of the scapulothoracic and glenohumeral articulations in conjunction with pronation attitude of the shoulder structures transfers the fulcrum from the shoulder joint to the elbow.

RADIAL PRONATOR SYNDROME

Here we introduce a pathologic entity which in our clinic we refer to as the "radial pronator syndrome" and which because of its frequency of occurrence, and its similarity of pain localization and clinical phenomenon closely simulates true epicondylitis. The condition is very refractory to routine therapy. It rarely responds to localized procaine block for either diagnostic or therapeutic features, and it is aggravated by manipulation and short-wave therapy.

Reference to anatomic texts will give us complete descriptions of the course and innervation of the radial nerve in the arm. We are mainly concerned at this time with that portion of the radial nerve as it presents itself after it winds around the medial to the lateral side of the humerus in a groove between the medial and lateral heads of the triceps brachii. At this point it pierces the lateral intermuscular system and passes between the brachialis and brachioradialis to the front of the lateral epicondyle, where it divides into a superficial branch and a deep branch. The superficial branch passes along the front of the radial side of the forearm to the commencement of its lower one-third; it lies at first slightly lateral to the radial artery, concealed beneath the brachioradialis. The deep branch of the radial nerve (n. interosseous dorsal or posterior interosseous nerve) winds to the back of the forearm around the lateral side of the radius between the two planes of fibers of the supinator, and is prolonged downward between the superficial and deep layers of muscles, to the middle of the forearm.

Extension of the elbow, pronation of the forearm, and flexion of the wrist and fingers make taut the fixed portion of the radial nerve along the groove of the humerus on to the fixed attachment of the deep (motor) branch of the nerve. Clinical tension of the nerve at that portion underneath the lateral wad of the elbow where the nerve winds itself about the neck of the radius is productive of pain and discomfort. There are localized pain and tenderness on careful palpation of the dorsal interosseous nerve. The mechanical irritation of the nerve becomes clinically manifested through sensory fibers, such as in deep sensation, position, and Allbutt's vibratory touch, or through tension on the radial nerve before the division into sensory and motor branches, with clinical manifestations indirectly placed on the sensory division of the nerve, which is cutaneous and articular. Aggravation by irritation or tension of this nerve branch readily precipitates the painful syndrome.

We have found that the nerve or nerve fibers which are made tense by the manner of passage through two muscles or tendinous attachment, fascia,

or ligaments, a rapid functioning or contracting juxtamusculature, are considered the cause of the pronator syndrome.

DIAGNOSIS

This is established primarily upon a history of repeated sudden tension of the extensors of the forearm and direct trauma to the lateral aspect of the elbow. The clinical findings are localized areas of tenderness in that region, particularly over the lateral condyle. There is no impediment to flexion or extension of the elbow. Pronation and supination are complete and asymptomatic. However, pronation in conjunction with a completely flexed wrist is symptomatic. Similarly, a fully pronated hand with a flexed wrist will produce pain at the last few degrees of flexion of the elbow. It is to be noted that in the pronator syndrome, local digital pressure when exerted on the profundus branch of the radial nerve as it dips into the supinator muscle of the forearm, will elicit the sharp pain experienced on precipitating exercises; moreover, the nerve usually can be palpated and feels enlarged.

TREATMENT

This may be summarized as follows: (1) Rest with a cast in the cock-up position to relieve the extensor pull. (2) Intensive thiamin and some multivitamin therapy. (3) Physiotherapy in the form of deep radiant heat followed by massage and exercises. Iontophoresis with Mecholyl, Histamine, or Procaine can be used. Paraffin baths have proved of merit. (4) Local infiltration with Procaine; or Hydrocortone followed by deep kneading or massage. (5) Manipulation designed to break up the adhesions or fixations by means of a sudden jerk on the elbow in a varus direction. (6) X-ray therapy. (7) Surgery.

The leading exponents of manipulation are Mills[3] and Cyriax.[4] Mills recommended jerking while the patient's elbow is fully extended with the forearm pronated and the wrist and hand flexed, in order to place the extensor carpi brevis on the stretch. Cyriax manipulated while the elbow is at a right angle, with the idea of making a partial or complete tear. With routine treatments of lateral epicondylitis, three weeks to three months usually are required to relieve the symptoms.

Osgood[5] reported good results from excision of the radial humeral bursa. Hohmann's[6] surgical procedure of stripping the distal extensor muscles of the forearm from the lateral epicondyle has given temporary relief, only to create an unstable elbow joint, as does the osteotomy.

FASCIOTOMY

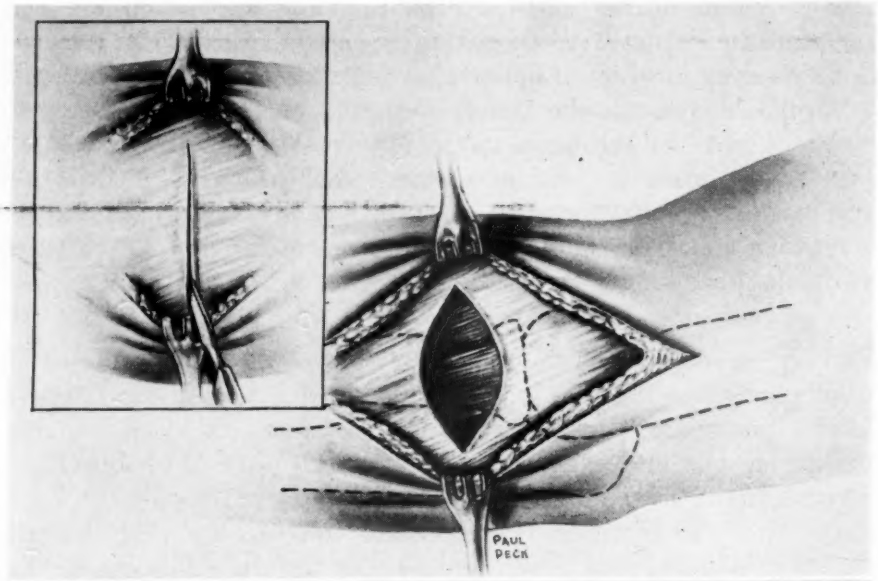
We believe that the fasciotomy, so ably used by Ober[7] on the thigh and by Bennett[8] on the medial epicondyle for a baseball elbow, is the procedure of choice. We have performed the fasciotomy in many cases, some of which have been followed for over five years, and have obtained complete relief of symptoms without recurrence.

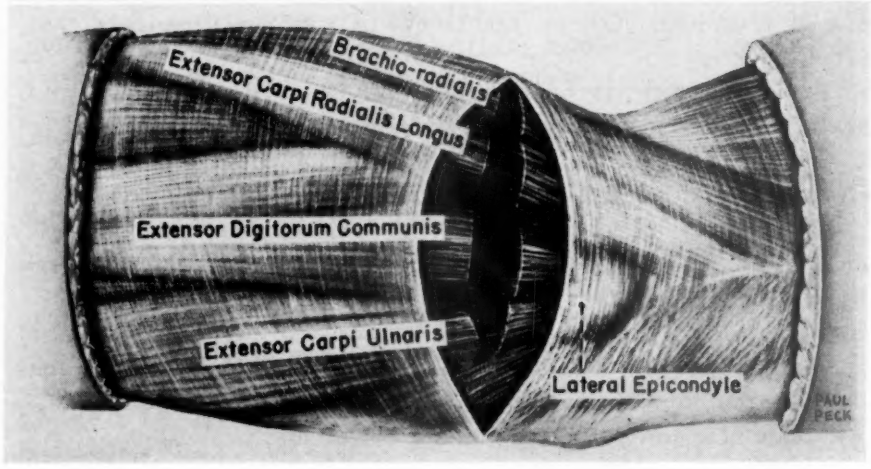
The procedure is graphically illustrated in the drawing in Fig. 3. The involved arm is draped out, and a transverse 2-inch long incision is made

two fingerbreadths distal to the lateral epicondyle over the "mobile-wad" laterally, including the intermuscular septae. Then a fascia and tendon sheath lysis is carried out as shown. In all cases the muscle bulges, owing to the tension of the fascial sheath. The subcutaneous tissues and skin are approximated by suture. A heavy surgical dressing and sling are applied.

The operation can be performed under local anesthesia, but general anesthesia is advisable in order to allow sharp flexion to completely relax the extensor aponeurosis.

A.





B.

Fig. 3.—*A*, Surgical exposure of the fascia; *B*, fascia and tendon sheath lysis.

The fasciotomy has given our patients immediate and complete relief of deep epicondylar pain, and they usually are able to return to full duty by the third postoperative week. The following case histories are representative:

CASE 1.—R. T. R., a 35-year-old Coast Guard machinist on the West Coast, had his left arm twisted in an assault in November of 1948. The extensor apparatus of the wrist and hand first became numb, then painful on motion, the pain beginning at the lateral

epicondyle and appearing in the extensor muscle bellies distally for some 3 to 4 inches. Later, the pain became localized in the lateral epicondyle and was aggravated by supination of the hand with full flexion, or by extension of the hand, increasing with flexion (Fig. 2). A diagnosis was made of epicondylitis and the patient was treated by heat and massage, procaine, and so on.

The condition did not improve, and the patient was never pain-free. He was transferred to the East Coast and came to the USPHS Hospital in March, 1949.

A brief period of physiotherapy and Novocaine diagnostic tests confirmed the diagnosis of epicondylitis. The "pronator syndrome" was ruled out. On May 10, 1949, a fasciotomy was performed which gave immediate and complete relief of symptoms. The patient returned to full duty on the first of July, 1949, and was followed repeatedly for about five years. The symptoms had not returned.

CASE 2.—A. T., a 46-year-old ship's steward, began to feel pain over the lateral epicondyle and about one inch distal to it ten months before admission. He attributed his symptoms to an injury received by striking his elbow against a door. Throughout the ten months following the incident he had felt severe pain over the lateral epicondyle on full flexion or extension of the hand or rotation (supination) of the forearm, or on carrying anything heavier than about one pound. Deck chipping or painting was particularly painful. He had been treated with physiotherapy, Novocaine injections, and rest, without relief.

On admission the patient's lateral epicondyle was found to be painful on passive full flexion or extension of the hand, and point tenderness was elicited over and distal to the lateral epicondyle. A fasciotomy gave immediate relief of pain, and follow-up has shown no sign of recurrence.

Fig. 4.—Manner of manipulation of the joints of the extremity in order to incite symptoms.

CASE 3.—C. L., a 52-year-old seaman, was admitted on July 10, 1946, with a history of pain on the lateral aspect of the right elbow of three weeks' duration. There was no history of trauma. The pain radiated from the elbow down the dorsal surface of the arm to the hand, and was aggravated by motion. At no time had the elbow been swollen. Examination revealed marked tenderness localized over the lateral epicondyle of the right humerus. The range of motion of all the joints of the forearm was full and painless, except that motion of the elbow increased the pain. Dorsiflexion of the wrist against resistance evoked

severe pain in the elbow. There was definite weakness of grip in the right hand, but no sensory changes were noted. X-ray examinations of the affected elbow revealed no abnormality.

Diathermy, cock-up splint, and Procaine infiltrations of the tender areas for a period of ten weeks produced no improvement, and, on Aug. 8, 1946, a fasciotomy in the region of the lateral epicondyle, as described, was performed. This gave notable relief of the pain and the patient was discharged on September 6 for convalescent physiotherapy for one more week, following which he was asymptomatic.

In Feb. 23, 1949, the patient returned to the hospital with a history of constant aching pain, in his left elbow this time, which had persisted for one month following a blow on the joint. He said the pain was similar to that experienced in 1946 in the right elbow, which was now asymptomatic. Examination of the left elbow showed the lateral epicondyle to be prominent and quite tender. There was full range of elbow motion, but supination was restricted to about 10 degrees. Full pronation with palmar flexion of the wrist (Fig. 4) produced severe pain about the lateral epicondyle in the region of the radiohumeral bursa. There were no sensory or vascular changes. X-ray examination of the part showed no bone or joint abnormality, but a chest roentgenogram demonstrated a pulmonary emphysema with old pleurisy of the left base.

Local procaine injections and whirlpool baths followed by cock-up splints for almost three weeks produced no improvement. On March 15, 1949, a fasciotomy in the area of the lateral epicondyle was performed and the radiohumeral bursa was excised. This was followed by relief of pain, and convalescent physiotherapy with whirlpool baths and graduate exercises was begun. Two weeks later the patient was discharged with no symptoms except a small area of hyperesthesia, about 2 by 2 cm., on the extensor portion of the forearm distal to the skin incision. Follow-up five years later has shown permanent and complete relief of symptoms.

REMARKS

A not infrequent differential phenomenon in lesions occurring near the site of the lateral epicondyle is the "pronator syndrome." This syndrome is due to a muscular stretch, tension compression of the profundus branch of the radial nerve during supinator muscle action. Its diagnosis must be ascertained before manipulation after the manner of Mills and Cyriax, and, if found to be a resistant neurological irritation, it may constitute one cause of failure to obtain relief of pain immediately after surgery.

SUMMARY

Painful lateral epicondylitis of the elbow has been completely relieved by fasciotomy of the extensor apparatus of the arm into the hand. A method of fasciotomy is described, which has given immediate relief of pain. Three representative case histories are reported, with a description of the syndrome. The pronator syndrome as a differential feature is discussed briefly.

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Case Reports

CARCINOMA OF THE INFRAPAPILLARY PORTION OF THE DUODENUM

Report of a Case and Review of the Literature

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PRIMARY carcinoma of the duodenum is an uncommon lesion. In a series of 350,286 autopsied cases collected by Eger,[3] the incidence was 0.033 per cent. In this same report, carcinoma of the duodenum represented 45.6 per cent of those found in the entire small bowel. The distribution of primary duodenal carcinoma as reported by Eger is as follows: First portion of the duodenum 23.9 per cent, second portion 61.9 per cent, third portion 12.1 per cent, entire duodenum 1.9 per cent. Kleinerman[4] reported similar figures in that 45 per cent of small bowel carcinomas originate in the duodenum. Of these, 22.5 per cent were found to be supra-ampullary, 59.2 per cent ampullary, and 18.3 per cent infra-ampullary.

In a recent review of the world literature, Odelberg[6] found only twenty reports of histologically proved adenocarcinoma of the infrapapillary portion of the duodenum treated by resection. Two cases were added by the author. Chadoff[2] subsequently has reported an additional case.

We have recently treated a case of infrapapillary adenocarcinoma of the duodenum by resection, bringing the total cases treated by this method to twenty-four.

CASE REPORT

A 72-year-old Negro woman entered the Second Surgical (Cornell) Division, Bellevue Hospital, with the chief complaint of epigastric "misery" of two years' duration. The patient had been in good health except for fifteen years of hypertension and a mild left cerebral vascular accident three years prior to admission. Two years prior to admission the patient noted the onset of mild epigastric pain, which came on one to two hours after meals and was relieved by bicarbonate of soda, but not by food. The pain progressed in severity and frequency. Four to five months before admission rapid filling of her stomach was noted, characterized by a feeling of hunger which could be satisfied by eating a small portion of food. One month before admission daily forced vomiting was utilized for relief of pain after alkali had lost its effectiveness. Spontaneous vomiting was denied, but frequently the patient regurgitated small amounts of her meals. During the week prior to admission the patient had eaten practically nothing and had taken limited amounts of fluid. The patient's weight prior to admission was 165 pounds and on admission was 135 pounds.

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Physical examination revealed temperature 37° C., pulse 80, respirations 16, and blood pressure 172/88. The patient was a well-developed, obese, dehydrated Negro woman in no acute distress, who showed evidence of weight loss. Grade II retinopathy was noted. The abdomen was soft, without distention. No solid organs or masses were palpated.

Laboratory data showed admission urine specific gravity 1.022, albumin 1 plus, sugar negative, acetone negative, bile negative. There were one to two red cells and two to three white cells per high-powered field. Admission hemoglobin was 13.5 Gm., red blood count 3.6 million, hematocrit 37, white blood cells 10.9, with 81 mature polymorphunuclear eosinophil leukocytes, bands none, lymphs 18, monos none, eosinophils none, basophil one. Platelets were noted to be adequate. The nonprotein nitrogen was 129 mg. per cent, CO_2 combining power 54 volumes per cent, chlorides 65 meq. per liter, the sodium 125 meq. per liter, and the potassium 2.8 meq. per liter. The vomitus and stools were positive for occult blood. The gastric analysis showed no free acid after histamine. A chest film was negative. Gastrointestinal x-rays showed an obstruction of the barium somewhere beyond the pylorus, but no definite diagnosis was made on this roentgenogram.

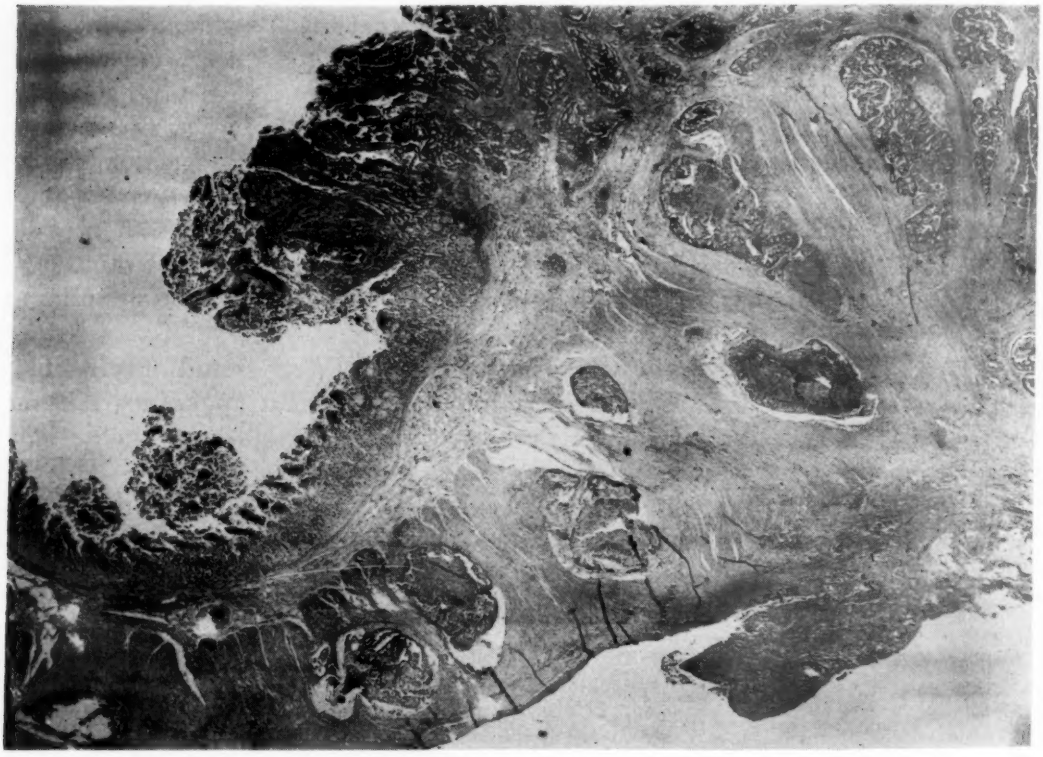

Fig. 1.—Photomicrograph showing transition from normal duodenal mucosa on the left to anaplastic adenocarcinoma involving all layers of the duodenum (×14; reduced ⅕).

Course.—The patient was kept on Wangensteen suction for ten days prior to operation. During this time the existing electrolyte imbalance was corrected by appropriate repair solutions. The nonprotein nitrogen gradually returned to normal. On July 14, 1954, twelve days after being admitted to the hospital, the patient underwent exploratory laporatomy and resection of an annular carcinoma of the last portion of the duodenum. The lesion was situated just proximal to the ligament of Treitz, and measured approximately 3 by 3 by 3 cm. An end-to-end duodenojejunal anastomosis beneath the mesenteric vessels reconstituted the bowel. During the procedure the common duct was cannulated in order to clarify the exact location of the papilla of Vater. An in-dwelling common duct T tube was

left in place and the operative area was drained. A week postoperatively copious amounts of brown-stained material were noted in the dressing. A catheter was placed in the drainage site and constant suction was applied after the diagnosis of a lateral duodenal fistula was made. The skin of the abdomen was protected with baker's yeast and tincture of benzoin. Following the development of this fistula the patient went into a situation of electrolyte depletion and dehydration which was gradually corrected. However, during this period of dehydration it was believed that acute renal failure had developed and the patient's NPN gradaully rose to 180 to 190 mg. per cent. It remained above 100 mg. per cent throughout the remainder of the postoperative course. Approximately two weeks following the first procedure, gastrojejunostomy and feeding catheter jejunostomy were performed. Following this the patient began to improve somewhat, but never regained full strength and vigor. On the seventh day after gastroenterostomy the patient developed high fever and multiple abscesses of the anterior abdominal wall which were incised and drained. Cultured microorganisms from these wounds were reported as *Aerobacter aerogenes, B. proteus,* Enterococcus, and *B. coli.* These wounds did well on local care and massive antibiotics, but never healed completely. Just prior to the patient's death, copious amounts of bright red blood were noted to be coming from the fistula and from a nasogastric tube. The blood pressure dropped to imperceptible levels before adequate restoration could be obtained. The patient died shortly following this episode of bleeding, on the thirty-sixth postoperative day. At autopsy a duodenal fistula, measuring 3 cm. in length, was demonstrated on the posterolateral margin of the duodenum at the anastomotic line. No bleeding point was discerned. No gross residual tumor was found.

Pathological Report.—Grossly, the tumor was a fungating annular lesion, measuring 3 by 3 by 3 cm., which almost completely occluded the duodenal lumen and involved all layers of the bowel wall. There were 5 cm. of normal duodenum proximal, and 5 cm. of normal jejunum distal to the mass. Two enlarged, firm lymph nodes were attached to the posterolateral surface of the duodenum. Microscopic examination revealed this tumor to be a highly anaplastic papillary adenocarcinoma. Many of the cells were multinucleated and showed indistinct outlines. Nests of mucin containing glands infiltrated all layers of the duodenum. Normal duodenal mucosa, containing submucosal Brunner's glands, merged with the proximal end of the tumor (Fig. 1). Adjacent lymph nodes were completely replaced by mucin-secreting carcinoma cells.

DISCUSSION

Lieber and associates[5] reported that in 30 cases of infrapapillary carcinoma of the duodenum 66 per cent were found in men. Eger[3] reported that the tumor occurs three times as frequently in men as in women. According to Eger's figures the sixth decade of life is the average and most frequent period when the disease occurs.

The symptoms and physical findings of carcinoma of the infrapapillary duodenum are nonspecific. In our case, as well as in those previously reported, the chief symptoms were upper abdominal pain, distention, vomiting, and weight loss. The duration of symptoms prior to operation ranges from ten days to three years, with an average of about four months. Our patient had symptoms for about two years. Physical findings were not helpful in establishing the diagnosis. Unless carcinoma of the duodenum is considered in the differential diagnosis of patients presenting this nonspecific clinical picture, the diagnosis will not often be made preoperatively.

Achlorhydria gastrica was demonstrated in our patient. This is an inconstant finding in most series reported. Lieber and co-workers[5] reported achlorhydria in 57 per cent of their cases.

Gastrointestinal roentgenograms generally suggest lesions in or about the distal stomach or duodenum but are by no means specific. X-ray studies demonstrated abnormalities of the duodenum in sixteen of nineteen cases in which roentgenograms were reported, although the diagnosis of duodenal tumor was made preoperatively in only three cases. Other diagnoses included duodenal strictures, duodenal dilatation, filling defect of pylorus, gastric carcinoma, irregular duodenum. In three cases x-ray findings were negative. In our case the roentgenograms were interpreted as pyloric obstruction due to chronic duodenal ulcer or carcinoma of the pyloric stomach (Fig. 2).

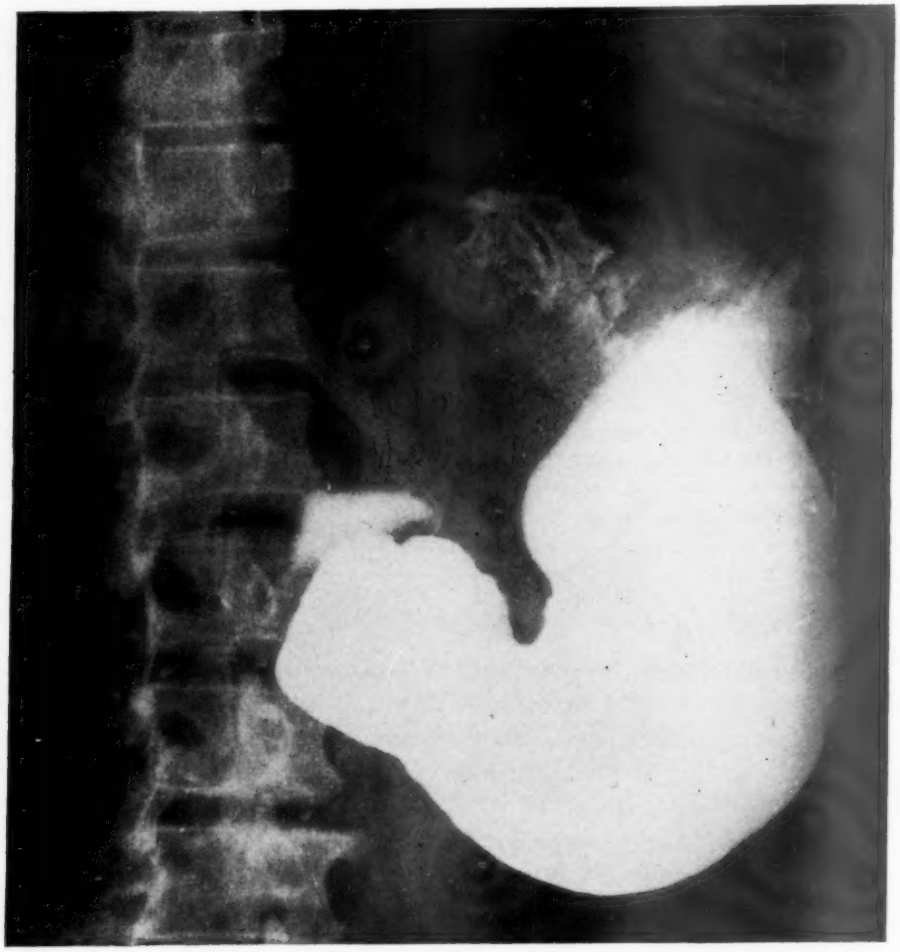

Fig. 2.—The operative gastrointestinal x-ray showing cessation of the flow of the barium in the first portion of the duodenum.

In view of the obscure nature of this disease and the lack of conclusive diagnostic methods to reveal this lesion, any patient who has persistent clinical and roentgenographic evidence of duodenal obstruction should be subjected to early operation.

Of the previously reported cases the vast majority were treated with simple resection and either end-to-end or end-to-side anastomosis. In two

cases gastroenterostomy was performed at the time of resection. In retrospect, this might have simplified the course in our patient had it been carried out with exclusion of the pylorus at the time of resection.

In only one of the twenty-four reported resected cases of infrapapillary carcinoma of the duodenum was a radical pancreaticoduodenectomy performed (Brunschwig and associates.[1] It is surprising that this operation has not been attempted more often, especially in those cases in which pancreatic invasion has been present. It was considered in our patient at the time of surgery, but because of her poor condition and advanced age a simpler procedure was thought more appropriate.

We would like to comment particularly upon the operative procedures used in treatment to emphasize certain points learned from our experience that might be helpful to others confronted with a similar situation. In summary, the following procedures are available and the choice will be governed by the general condition of the patient and the operative findings.

1. Gastroenterostomy. A palliative procedure indicated for nonresectable lesions.

2. Resection with end-to-end or end-to-side jejunal-duodenal anastomosis. This procedure seems indicated in lesions which are small and have not invaded into the pancreas, and in which an adequate margin of uninvolved duodenum separates the tumor from the common duct and ampulla of Vater.

3. Resection with gastroenterostomy and pyloric exclusion. Resection with end-to-end anastomosis and gastroenterostomy alone does not seem rational, but, in cases where the end-to-end suture line is tenuous, exclusion of the pylorus with gastroenterostomy has a definite place. The grave consequences of a lateral duodenal fistula can be avoided if there is dissolution of the suture line. If a fistula should develop, the "end" variety is better tolerated and closes spontaneously more readily.

4. Radical pancreaticoduodenectomy. This operation seems indicated in extensive lesions with invasion of the pancreas and/or common bile duct. This procedure will have wider application in the future than it has had in the past, with the advent of modern surgical techniques and methods of anesthesia.

The over-all operative mortality in the reported resected cases has been about 20 per cent. However, the long-term prognosis is reasonably good. The tumor is uniformly an adenocarcinoma, and distant metastases are generally a late occurrence.[4] Odelberg[6] presented follow-up reports on five patients living and apparently in good health three years after resection, and two of the five survived eighteen years without evidence of recurrence. Unfortunately, the follow-up studies are incomplete in many of the patients who survived resection.

SUMMARY

1. A case of infrapapillary carcinoma of the duodenum treated by resection is added to the literature bringing the total number of reported cases to twenty-four.

2. The diagnosis should be considered preoperatively in patients presenting upper abdominal pain, distention, vomiting, and weight loss when roentgenograms reveal obstruction of the third portion of the duodenum and/or dilatation of the first and second portions.

3. Local resection with an end-to-end anastomosis seems adequate when feasible, but gastroenterostomy with pyloric exclusion should be added when the safety of the anastomotic line is questionable. Radical pancreaticoduodenal resection should be considered in invasive cases.

4. Although significant five-year survival figures cannot be obtained due to the paucity of cases, the long-term prognosis in patients undergoing resection seems good.

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LIPOTHYMOMA

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WITH the increasing use of the routine hospital admission chest roentgenogram and of the mass survey, a number of rare benign thymic tumors have been disclosed. These tumors include adenoma, fibroma, lipoma, myoma, and lipothymoma. Bigelow and Ehler[2] introduced the term "lipothymoma" to identify a benign tumor containing an admixture of thymic elements with lipomatous tissue, thus differentiating it from the more common lipoma which is devoid of lymphoid tissue and of Hassall's corpuscles. To Rubin and Mishkin's[8] four collected cases is added the following case report of a lipothymoma.

CASE REPORT

N. C., a 24-year-old white married woman was admitted to the Thoracic Service of The City Hospital of Akron on Oct. 16, 1954, for investigation of an asymptomatic large radiopaque mass in the right hemithorax. The lesion was found on a routine admission chest roentgenogram (Fig. 1) taken at a local sanatorium where the patient was to receive shock therapy for schizophrenia. No prior chest x-ray film had ever been taken. There was no history of any sign or symptom referable to the thorax or upper abdomen; however, the patient had noted vague distress in this area subsequent to roentgen disclosure of the chest disease. In the past nine months the patient's weight dropped from 105 pounds to 87 pounds. During this time she had been progressively more depressed and stated that she had had no appetite.

The past history and family history were notable only for the occurrence of pneumonia on two occasions during childhood. She was a gravida iii, para ii, having had one spontaneous early abortion.

Physical examination revealed a healthy, thin, cooperative, intelligent, quiet, white woman in no distress. Her stature was small and asthenic. There was no cyanosis, dyspnea, abnormal chest shape, nor clubbing of the fingers. Except for dullness and absence of breath sounds over the right base, the physical examination was noncontributory. Prior to admission to the hospital the patient had been studied elsewhere and a needle aspiration of the thoracic mass had been "dry." A pneumoperitoneum carried out at the same time was interpreted to indicate that the mass was supradiaphragmatic.

The preoperative diagnosis was "right anterior lower thoracic malignancy, probably a sarcoma of the pleura."

On Oct. 18, 1954, a right thoracotomy was performed. Filling the lower 60 per cent of the hemithoracic cavity was a homogeneous, yellow, encapsulated, fairly soft, fatty tumor. This extended from the inferior pole of the right portion of the thymus gland distally to where it covered most of the diaphragm. The tumor derived its blood supply from multiple small arteries and veins in the region of the thymus and was readily resected with the isthmus and right lower ramus of that organ. It was impossible to tell where the thymic tissue left off and the tumor began. However, it was obvious that the tumor contained, in the main, tissue far more amorphous than that found in the thymus. Following tumor resection, the expanded right lung was pink, practically devoid of anthracotic pigment, and it did not completely fill the hemithorax. The resected tumor (Fig. 2) was

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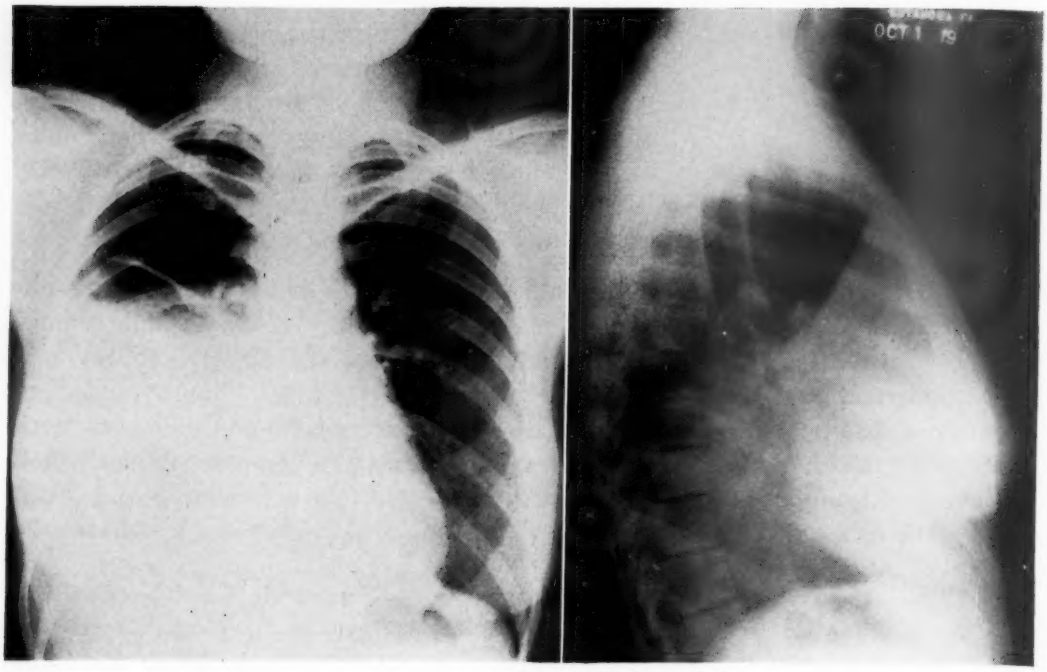

A. *B.*

Fig. 1.—*A* and *B*, Posteroanterior and lateral chest roentgenograms taken prior to surgery.

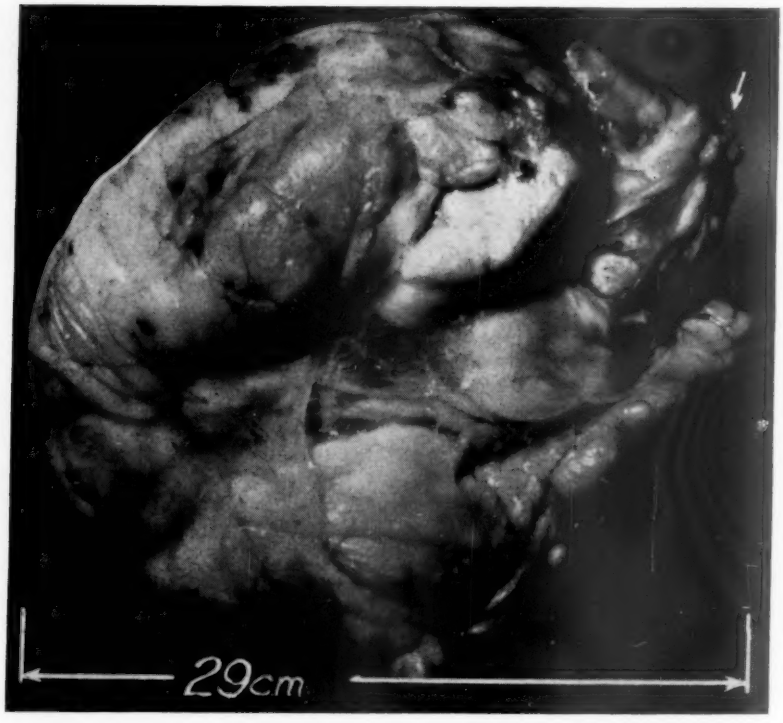

Fig. 2.—Resected lipothymoma. Arrow indicates attachment to thymus.

B.

A.

Fig. 3.—*A* and *B*, Low- and high-power photomicrographs of specimen showing normal thymic elements interspersed in adipose tissue.

tan to yellow in color, encapsulated, 32 by 26 cm. at the greatest diameters, and triangularly shaped. At the apex of the triangle was the thymus. The tumor weighed 5 pounds. Histologic section (Fig. 3) revealed a mass of adipose tissue with relatively large cells and few septa. There were numerous nests of thymic tissue disseminated through the adipose tissue.

Convalescence was uneventful and the patient was discharged from the hospital Oct. 26, 1954. A chest roentgenogram taken in December, 1954 (Fig. 4), showed a relatively normal thorax.

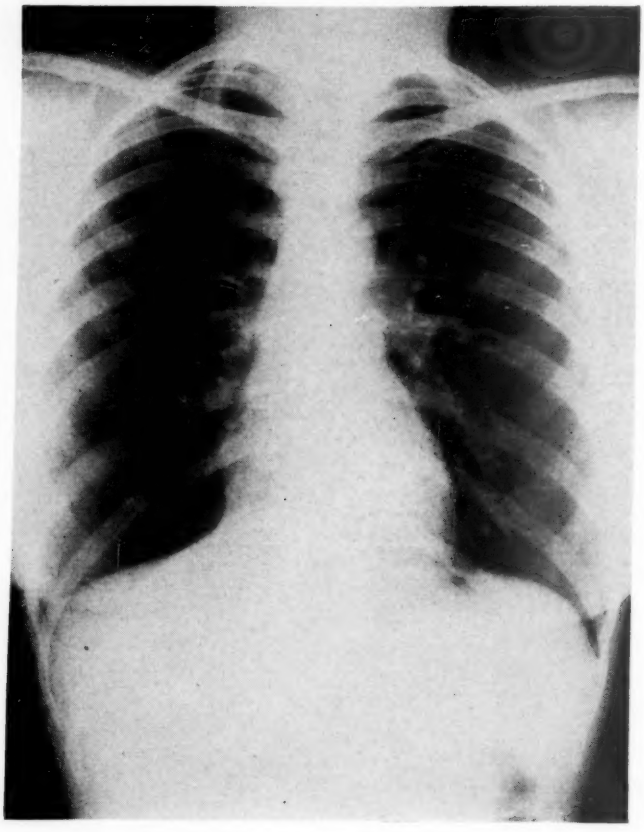

Fig. 4.—Postoperative chest roentgenogram.

DISCUSSION

With the collected findings of anorexia, weight loss, emotional depression, and dullness over the right lower hemithorax coupled with the roentgen evidence of a large homogeneous mediastinal mass, it seemed logical to consider the tumor both malignant and the total cause of the patient's disability. Thoracentesis, diagnostic pneumoperitoneum, and multiple careful physical and roentgen examinations were performed in an effort to establish the nature of the alleged malignancy and thus be able to finesse thoracotomy. Roentgen therapy was proposed as an alternate course but was successfully inveighed against by the thoracic medical-surgical group. Although this tumor was asymptomatic, it is reasonable to assume that, with continued growth, it would have caused increasing intrathoracic compression and would have become manifest by mediastinal compression.

The almost complete absence of symptoms in this case is consistent with McCorkle's[7] observation that a thoracic lipoma may cause no symptoms. Conversely, marked symptoms may develop due to the distressing intrathoracic compression secondary to a large tumor.

The preoperative diagnosis is not commonly made because of the absence of any specific symptom complex and because of the bizarre radiographic appearance of some of these tumors. In Keeley's[6] review of fifty-eight cases, only six were diagnosed prior to operation, thirty-three were diagnosed at operation, sixteen at autopsy, two by biopsy, and one by means unstated. Of the thirty-eight cases explored, thirty survived and were apparently cured; eight cases died, sepsis being the common cause of death.

Heuer,[5] in 1933, in a collective review of thirty-one cases of lipoma of the thorax, focused attention on the various locations of such tumors. In this series, there were nine hour-glass or dumbbell type lipomas composed of two masses, an intrathoracic component connected by a constricted portion or isthmus to an extrathoracic mass; there were four mediastinal lipomas extending into the neck and eighteen true intrathoracic lipomas. True intrathoracic lipomas are not common; Blades[3] encountered only three in a series of 109 mediastinal tumors. After the further classification of lipomas of the thymus into lipoma and lipothymoma by Bigelow and Ehler,[2] Rubin and Mishkin,[8] in 1954, reviewed three cases from the literature and one of their own which satisfied the histologic requirements for a lipothymoma. This latter tumor, by combining the parenchymatous and stromal elements of the thymus and of fatty tumors, would appear to be a true benign neoplasm. It is conceivable, however, that a lipoma might develop within the confines of the thymus gland and in growth separate the normal parenchymatous elements of that organ so that they were markedly dispersed throughout the fatty tissue. Certainly in a lipothymoma the thymic tissue is dispersed thinly throughout the neoplasm and one might question whether there was any absolute increase in total thymic elements as a result of the new growth. In the case herein reported, the neoplasm was an obvious separate entity arising from the very lowermost portion of the right ramus of the thymus gland, and it satisfies the microscopic requirements of lipothymoma.

The four reported cases of lipothymoma described in detail by Rubin and Mishkin[8] include, in brief:

1.—A 13-year-old boy. Preoperative diagnosis: intrathoracic lipoma. Successful resection by Andrus and Foot[1] of left chest tumor, weight 2,235 grams, measuring 26 by 24 by 7.5 cm. Histology: characteristic thymus tissue with excessive fat.

2.—A 10-year-old white girl. Symptoms: paroxysmal cough of ten weeks' duration. Successful removal by Bigelow and Ehler[2] of tumor weighing 170 grams, measuring 12 by 9 by 4.5 cm. Histologic appearance as in Case 1. Five-year survival without recurrence.

3.—A 14-year-old boy. Asymptomatic survey case. Successful resection by Gross[4] of left thymic tumor extending over pericardium. Histologic appearance same as in Cases 1 and 2.

4.—A 19-year-old Mexican girl. Signs limited to exertional chest pain and dyspnea and apparent cardiac enlargement since age 14. Successful removal by Rubin and Mishkin[8] of tumor weighing 750 grams, measuring 20 by 14 by 10 cm. Histologic sections same as in Cases 1, 2, and 3.

Two of the five reported patients were asymptomatic; the others had symptoms referable to tumor compression. None had symptoms of myasthenia gravis.

It is interesting to speculate as to the duration of growth of the five reported lipothymomas. Due to the slow growth and adaptability of this type of tissue to conform to any enclosing space, it is conceivable that tumors of this histologic type grow over a period of several years and may prevent the normal development of contiguous organs. Further credence is given this contention by the case herein reported when one notes the obvious disparity between the small right lung when completely ventilated and the total volume of the right hemithorax.

The value of routine admission and survey chest roentgenograms is again manifest in such a case.

SUMMARY

To the four cases of lipothymoma already collected in the literature is added that of a 24-year-old asymptomatic white woman whose tumor was found on a routine roentgen chest survey examination and after successful removal was identified as a lipothymoma.

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ADDENDUM

Since the preparation of this manuscript our attention has been directed to 5 additional cases of lipothymoma. Guilfoil and Murray[3] reported the finding in a 22-year-old white man of a 540 gram tumor and reviewed Hall's[4] report of the autopsy finding of a lipothymoma in a 47-year-old man. In addition, they included the case reported by Schanher and Hodge[5] of a 35-year-old woman whose thorax was explored because of the presence of a symptomatic mediastinal tumor—a lipothymoma; and a review of the case reported by Bariety and Coury.[1] The fifth reported case was that of Dailey[2] who observed a lipothymoma in an adult.

Record could thus be found of 10 lipothymomas, 4 in children and 6 in adults.

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LINGUAL GOITER

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THYROID gland tissue anomalies occurring above the region of the hyoid bone are of interest to the surgeon because of their embryonic origin, the various parenchymatous changes that may occur, and the technical problems encountered in their surgical treatment.[5] These anomalies may occur in any area from the base of the tongue to the suprasternal notch at or near the midline.[11] This discussion takes into consideration thyroid gland tissue observed in the region of the foramen cecum (lingual goiter), within the substance of the tongue (intralingual goiter), and above the hyoid bone in front of the larynx (sublingual goiter) (Fig. 1).

Hickman,[7] in 1869, was apparently the first to describe a congenital tumor at the base of the tongue which, histologically, was found to be of thyroid origin; this case was authenticated by Montgomery.[10, 11] In 1888, Bernays[1] removed a lingual thyroid gland tumor, substantiated by histologic examination, through a median pharyngotomy incision. In 1935, Montgomery[10, 11] made an extensive review of lingual goiters reported in the literature; he found 242 cases and reported one from his own experience at that time.

A questionnaire was sent to members of the American Goiter Association and leading surgeons of the country requesting a report on their experiences with this problem. One hundred ninety-six cases were reported on questionnaires returned, all of which had been confirmed by histologic examination of tissue removed. A complete report on the replies to this questionnaire is contained in an article to be published at a later date. The purpose of this report is to review five cases of lingual goiter operated upon by the author and to illustrate the two techniques utilized in their removal.

EMBRYOLOGY

A detailed discussion of the embryology of the head and neck and anomalies which may occur therein has been presented previously[17] only the practical points in the development of lingual and sublingual goiters are considered here.

The thyroid gland is derived from the medial diverticulum which appears on the summit of the tuberculum impar in approximately the eighth week of fetal development; later it is observed in a furrow immediately behind the tuberculum. Its growth is downward and backward as a tubular duct which later becomes the thyroglossal duct. The distal end of the duct bifurcates to become the isthmus and lateral lobes of the thyroid gland. The thyroglossal duct is represented at its upper end by the foramen cecum at the base of the tongue, and the lower portion becomes the pyramidal lobe of the thyroid gland.

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INCIDENCE

Gruber[6] reported finding thyroid gland tissue in abnormal or aberrant positions in 10 per cent of routine post-mortem examinations.

During a period of time when 1,309 thyroidectomies were performed by the author, five goiters were encountered in the lingual area and five in the sublingual area between the base of the tongue and the hyoid bone. Three of the lingual goiter patients were female and two were male; their ages ranged from 3 to 34 years. Four of these cases were observed before the advent of radioactive iodine (I^{131}); consequently it could not be determined, except by clinical examination, whether or not additional thyroid tissue was present.

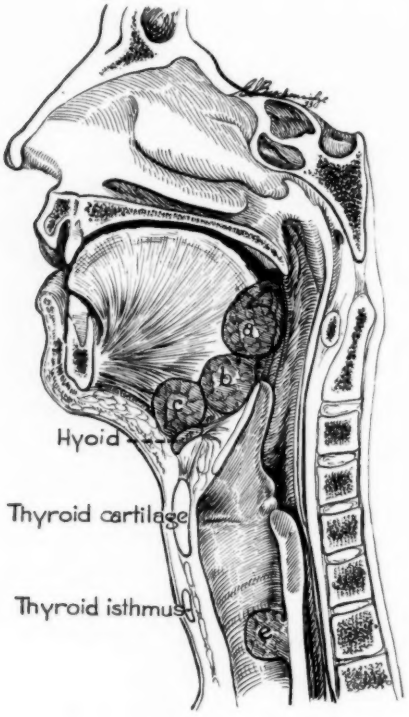


Fig. 1.

Fig. 2.

Fig. 1.—*a*, Thyroid tissue located in the region of the foramen cecum; *b*, thyroid tissue located within the substance of the tongue; *c*, thyroid tissue located in the sublingual area; and *e*, nodule of thyroid tissue on posterior tracheal wall opposite fourth tracheal cartilage.

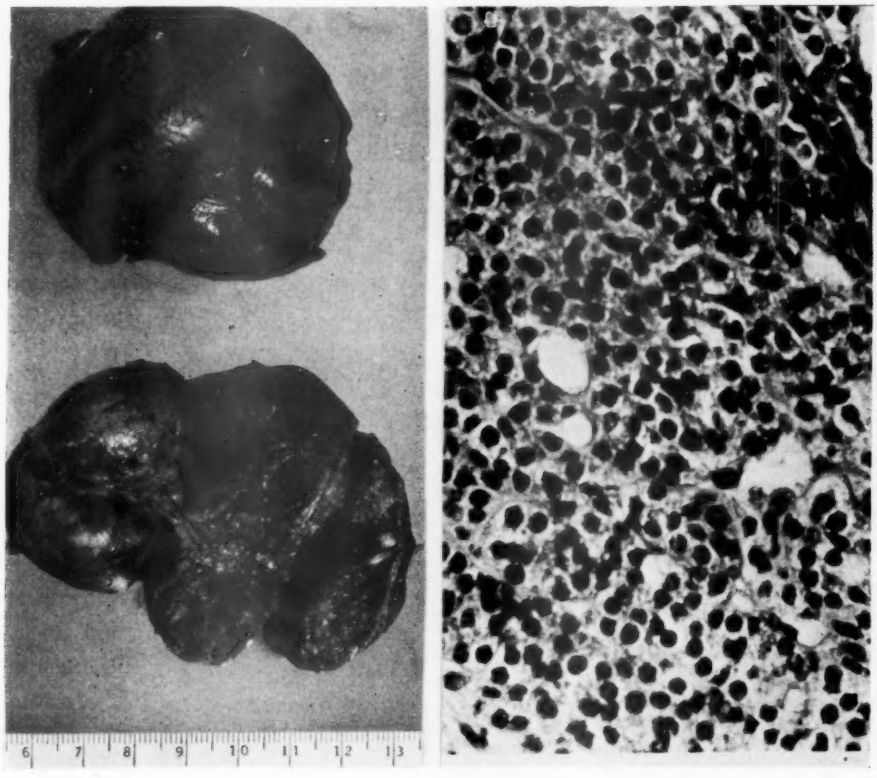
Fig. 2.—Three-year-old girl with lingual goiter 2 cm. in diameter. Growth is lateral to midline.

SYMPTOMS AND PATHOLOGY

The symptoms of lingual goiter in the five patients varied in accordance with the size of the tumor and age of the patient.[5, 10] Two patients had voice changes; one showed a marked change when the tumor almost filled the pharynx. Four patients complained of having interference with deglutition, dysphasia, and orthopnea.[3] In one patient, a 34-year-old woman, there was rather severe hemorrhage during the latter months of pregnancy resulting from ulceration of the buccal mucous membrane over the thyroid tumor. In two patients, the

tumors were of sufficient size to prevent normal motion of the tongue and acted as barriers to the passage of solid food. All five patients complained of choking attacks and fullness in the throat.

The lingual thyroid tissue removed in these five patients was similar to that found in the thyroid gland of individuals in the same age group.[5] There was no evidence of toxicity in any of the five patients. In one instance there were marked hyperplasia and hypertrophy in a 34-year-old woman during her seventh month of gestation. Histologic section of this patient's tumor showed normal thyroid tissue and tissue similar to parathyroid gland tissue (Fig. 3). One section of another patient's tumor also had the appearance, histologically, of parathyroid tissue. It is possible that the parathyroid gland may be associated with lingual goiter.



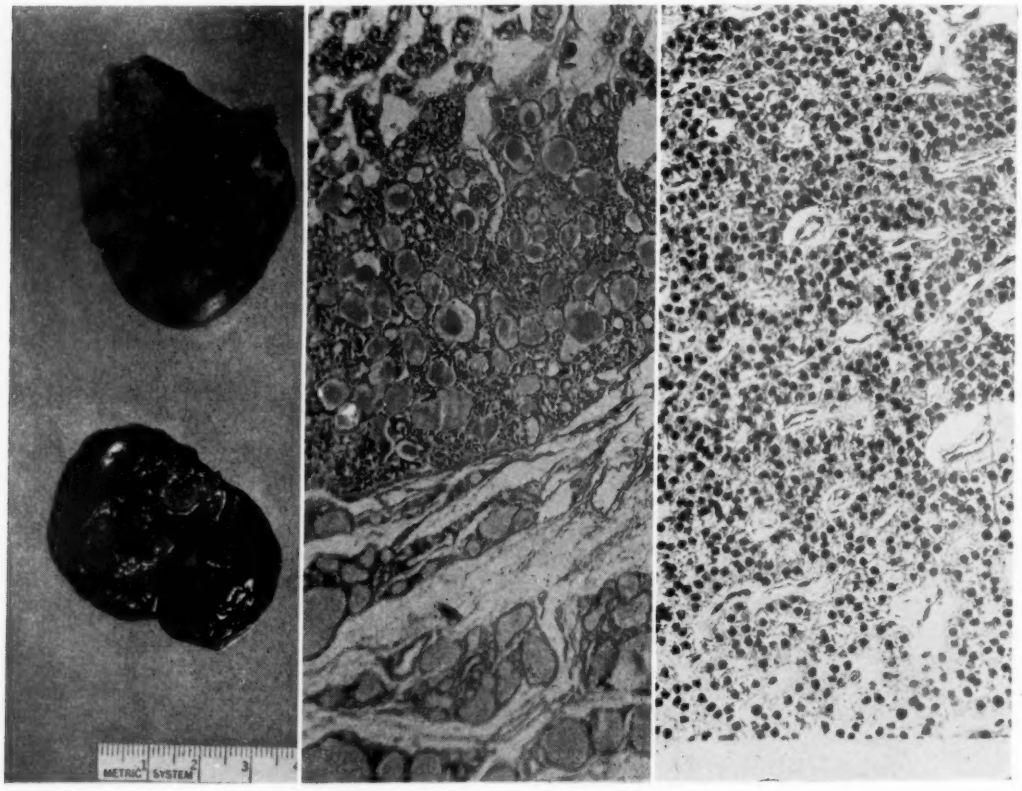
A. *B.*

Fig. 3.—*A*, Specimen of large lingual thyroid removed from 34-year-old woman; *B*, photomicrograph showing normal size follicles filled with colloid.

In two of the five cases of lingual goiter, the tumors were located within the substance of the tongue. In each case no tumor was visible on the mucosa of the tongue in the region of the foramen cecum, but there were fullness and thickness of the base of the tongue with a pronounced enlargement in the submental area of the neck.[13]

One of these patients, a white woman 28 years of age, complained for a period of several years of difficulty in swallowing, choking attacks, moderate interference with deglutition, and voice changes. Her family observed a slight fullness in the submental area. She had been examined repeatedly elsewhere without the cause of her symptoms being detected and had been treated for hypothyroidism with thyroid extract for several years. On self-examination, the patient observed an induration within the substance of the tongue which she called to the attention of her family physician who referred her to me for diagnosis and treatment.

Examination of this patient revealed a well-developed, well-nourished woman. Her general physical condition was negative with the exception of fullness in the submental area of the neck and thickness and hardness within the substance of the base of the tongue. The patient was a short, thick-necked individual; no thyroid tissue could be palpated in the normal position of the thyroid. A probable diagnosis of intralingual goiter was made.



A. *B.* *C.*

Fig. 4.—*A*, Specimen of lingual thyroid, 14-year-old girl; *B*, photomicrograph showing normal-appearing thyroid follicles; *C*, photomicrograph showing typical appearance of parathyroid tissue. This type tissue was observed in two of five cases presented here.

The operative procedure was carried out through a transverse incision, approximately 10 cm. long, above the hyoid bone. The upper and lower skin flaps were dissected widely and a longitudinal incision was made in the mylohyoid and geniohyoglossus muscles. A hard nodule was found within the substance of the base of the tongue. The lingual muscles were retracted exposing an incapsulated nodule which was not found to extend to the mucous membrane of the oral cavity. The nodule was excised and immediate frozen section revealed papillary adenocarcinoma of thyroid gland origin (Fig. 5).[9, 15] There were no palpable nodes in the neck. The longitudinal incision in the mylohyoid and geniohyoglossus muscles

A. *B.* *C.*

Fig. 5.—*A*, Photomicrograph showing intralingual thyroid tumor, 28-year-old woman. Normal thyroid follicles varying in size contain colloid material; *B*, enlarged photomicrograph showing above; *C*, photomicrograph showing papillary adenocarcinoma.

was closed with interrupted sutures of fine chromic catgut. A suprahyoid neck dissection was carried out and no malignant cells were found in any of the 24 lymph nodes in the resected specimen. The patient made an uneventful convalescence; the preoperative symptoms disappeared and there has been no evidence of recurrence of the tumor after eight years.

REMOVAL OF LINGUAL GOITER THROUGH INTRAORAL ROUTE

Intratracheal anesthesia, with the tube inserted through the nose, is the anesthesia of choice in the removal of lingual and intralingual goiters. The pharynx is packed off well with a moist pack to prevent blood and secretions from entering the bronchial tree. Pentothal sodium, nitrous oxide, and oxygen are used throughout the operation to permit the use of electrosurgical current. Two heavy silk sutures are placed through the tip of the tongue; the mouth is opened widely and the tongue pulled forward. A large curved needle is used to place heavy silk sutures through the substance of the tongue beginning posteriorly to the tumor on either side. The sutures are placed sufficiently deep so that the

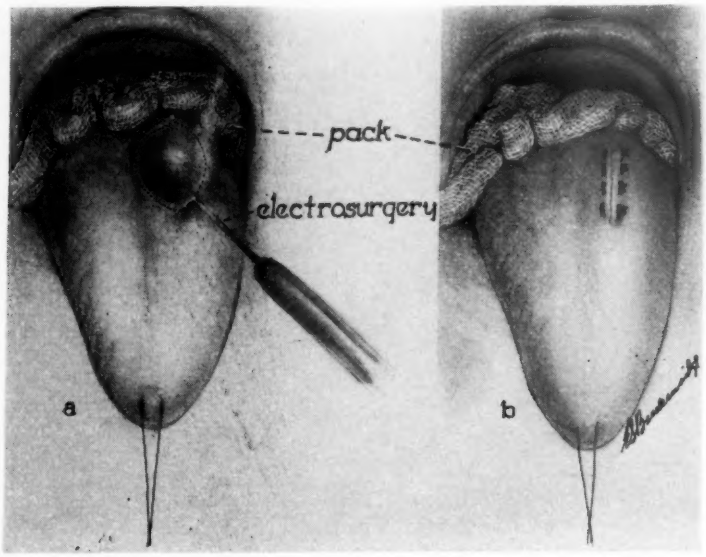


Fig. 6.—Technique showing removal of lingual goiter through intraoral route. Heavy silk sutures are placed through tip of the tongue after administration of intratracheal anesthesia; the pharynx is packed off with a moist pack to prevent secretions and blood from entering the bronchial tree. An elliptical incision is made around beneath the thyroid nodule with electrosurgical cutting current. Bleeding areas are coagulated. The defect is closed with mattress sutures of heavy black silk to eliminate all dead space and prevent postoperative hemorrhage.

tumor can be excised without destroying them. The ends of the sutures are caught with hemostats. An elliptical incision is made well around and beneath the tumor mass (Fig. 6) with an electrosurgical cutting current which reduces hemorrhage to a minimum. Any oozing is controlled by drawing the silk sutures taut and tying them. Additional chromic 0 catgut sutures are placed through the wound edges to obliterate all dead space and close the defect. Two patients treated with this technique made uneventful convalescenses and were discharged from the hospital on the fifth and sixth postoperative days. The silk sutures were removed on the tenth postoperative day.

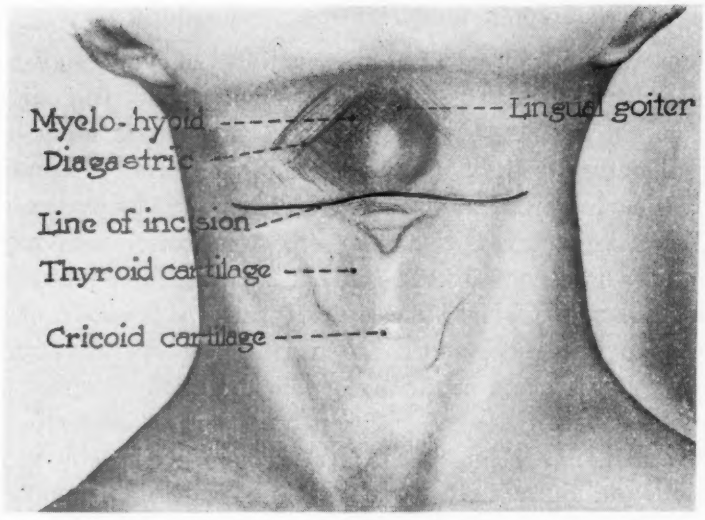


Fig. 7.—Operative technique for removal of lingual and intralingual goiter through median pharyngotomy incision. Transverse incision above the hyoid bone extends to the anterior border of the sternomastoid muscle on each side. Skin flaps are dissected upward exposing the lingual muscles.

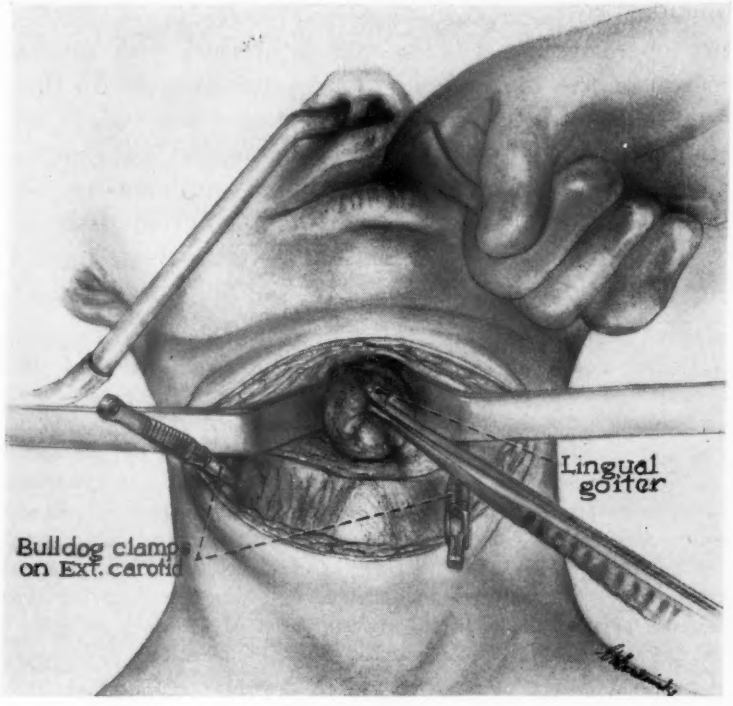


Fig. 8.—The external carotid arteries are dissected out on each side and a rubber-shod bulldog artery clamp is placed on each external carotid artery. The mylohyoid and geniohyoglossus muscles are opened in the midline. The finger of an assistant is placed in the patient's mouth well down on the posterior area of the tongue to assist in delivering the tumor. The lingual mucous membrane is closed with interrupted fine chromic catgut sutures. The geniohyoglossus and mylohyoid muscles are closed with fine interrupted chromic catgut sutures. The bulldog artery forceps are removed from the external carotid arteries. The mid-cervical fascia is closed with fine interrupted mattress sutures of silk. One rubber tissue drain is left within the depth of the wound.

MEDIAN PHARYNGOTOMY TECHNIQUE

Removal of lingual goiter using the median pharyngotomy technique was first performed by me in 1944 to remove a very large lingual goiter which measured 8 cm. in diameter.[7] A transverse incision is made in the suprahyoid area, following a crease in the neck, and is extended laterally to the anterior border of each sternomastoid muscle (Fig. 7). The platysma muscle and midcervical fascia are severed. The sternomastoid muscle and jugular vein are retracted laterally on each side. The internal carotid artery is dissected out at the bifurcation. A rubber-shod bulldog artery forceps is placed on each external carotid branch to prevent hemorrhage during the operative procedure.[2] A longitudinal incision is made in the mylohyoid and geniohyoglossus muscles; the edges of the muscles are retracted sufficiently to permit the removal of an intralingual or lingual goiter (Fig. 8). After excision of the goiter, if it is in the lingual position, the mucous membrane is closed with 0 chromic catgut sutures obliterating the wound. The lingual muscles are closed with interrupted chromic catgut sutures. The bulldog artery forceps are removed from the external carotid arteries; the cervical fascia is closed with fine cotton sutures and the skin with interrupted mattress sutures of silk. A Penrose drain is left within the substance of the lingual muscles and brought out through the most dependent part of the wound.

These two operative procedures have been used with satisfaction in the operative removal of five lingual and intralingual goiters. In three of the five patients, the lingual and intralingual thyroid tissue removed, in all probability, represented the entire amount of thyroid tissue present since none could be palpated in the cervical area of the neck. Thyroid extract was required to control hypothyroidism following removal of the lingual thyroid tissue in these three cases. In two patients, cervical thyroid lobes were palpated and there was no evidence of hypothyroidism after removal of the lingual goiters.

The most recent case operated upon was a 3-year-old Mexican girl observed in 1953 with a diagnosis of lingual thyroid tissue made by her attending physician.* The parents had observed that the child had difficulty in talking and swallowing, especially solid foods. Upon careful examination,* a nodule was found on the base of the tongue near the midline in the region of the foramen cecum. When the child was seen by the author, an elevated nodule 2 cm. in diameter was found and the initial diagnosis* was confirmed. No thyroid tissue could be palpated in the cervical area of the neck. Under intratracheal anesthesia, the lingual goiter was removed by the intraoral route described previously. The patient made an uneventful recovery but demonstrated clinical evidence of hypothyroidism and was placed on thyroid extract to control the deficiency. Studies made using radioactive iodine did not demonstrate thyroid tissue in the cervical area of the neck or other regions of the body. The child has shown normal growth and is in excellent health.

SUMMARY AND CONCLUSION

Five cases of lingual and intralingual goiter are reported. The treatment administered consisted of excision of the tumors through the intraoral route in two cases. The tongue was pulled forward; the pharynx was packed off after

*Dr. R. N. Graham, Del Rio, Texas.

insertion of an intratracheal tube. An elliptical incision was made around the tumor with an electrosurgical cutting current and the tumor enucleated. The defect in the substance of the tongue was then closed with interrupted heavy silk sutures.

The tumor was removed through a median pharyngotomy incision in three cases. A transverse incision was made through the skin in the suprahyoid area. The external carotid arteries were dissected out on each side and a rubber-shod bulldog artery forceps was placed on each external carotid artery permitting the operative procedure to be carried out with very little hemorrhage. A longitudinal incision was made through the muscles of the tongue. In one patient, the tumor at the base of the tongue was removed in this manner because of its large size. In the other two patients, the tumor was located within the substance of the tongue. In one of these, a papillary adenocarcinoma was encountered in a well-encapsulated intralingual thyroid tumor. A suprahyoid neck dissection was carried out; no positive nodes were found in the resected specimen. This patient has been followed for eight years with no clinical evidence of recurrence of the tumor.

There were no serious complications following these operative procedures and no recurrences of the tumors. Three patients were required to take thyroid extract to control hypothyroidism. The other two had sufficient cervical thyroid tissue to take care of their requirements.

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INDUCED HYPOTENSION IN SURGERY OF COARCTATION IN ADULTS

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SINCE the first reports of Crafoord and Nylin[5] and Gross and Hufnagel[8] ten years ago, sufficient experience has been accumulated to establish the resection of the obstruction and immediate anastomosis in coarctation of the aorta as a completely acceptable procedure in most patients with this abnormality. Gross[9] in 1953 summarized his series of 270 cases. His report and those of others[3, 4] further corroborated the conclusion that in the absence of serious valvular disease or myocardial damage surgical correction of coarctation should be offered in practically all cases.

Many of the early complications and failures are now avoided by the use of homografts[10] to overcome the defect resulting from the excision of a relatively long segment of vessel. This may be indicated because of the extent of the coarctation or because a tear or aneurysm of an intercostal artery necessitates resection of more than the site of the obstruction. In older patients, the inelasticity of the aorta may interfere with the approximation of the ends for a safe anastomosis despite the resection of a short segment.

With the problem of a long defect overcome by the use of homografts, there remains the ever-present hazard of serious and occasionally fatal hemorrhage during the manipulation of vessels of this size in which the pressure may be unusually high, particularly in adult cases. In some instances, it has been necessary to abandon attempts to resect the coarctation due to foreboding possibilities of fatal hemorrhage or to retreat as soon as hemorrhage has been brought under control.

With the introduction of ganglion blocking agents which induce hypotension and with the increasing use of these agents in combination with general anesthesia,[13] their use in the surgery of large vessels appears to be quite logical. Glenn and associates[7] have used hypotension in the surgery of patent ductus arteriosus in adults and in the resection of aortic aneurysm. Hypotension has been used in combination with hypothermia by Julian and his associates[11] in a series of aortic resections, all but one of which were for coarctation. We wish to present three consecutive case histories of male patients, aged 31, 21, and 28 years, in which hypotensive agents were used during operation for resection of coarctation.

Trimethaphan camphorsulphonate (Arfonad) has been obtained through the courtesy of Dr. M. T. Schiffrin of Hoffmann-La Roche, Inc.

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CASE REPORTS

CASE 1.—V. P., a 31-year-old, 200-pound former Golden Gloves boxing champion, fought professionally, winning 19 of 22 bouts, before being disqualified because of an "athletic heart" and hypertension. He was later rejected for military service for the same reasons. Early in 1954 he was admitted to the hospital because of cerebral symptoms occurring two weeks after a wrestling bout. Residual blindness and deafness on the left were the major findings. These may have been due to a cerebral vascular accident. The blood pressure in the arms was 182/84 and in the legs 130/?. The chest roentgenogram showed a dilated and bowed subclavian artery, a notch in the left border of the descending aorta, notching of the fifth, sixth, seventh, and eighth ribs on the right, and the sixth and seventh ribs on the left, and cardiac enlargement due principally to a large left ventricle. The electrocardiogram disclosed left ventricular hypertrophy and interventricular conduction defect of the type associated with hypertrophy. An operation was performed on March 31, 1954.

Preoperative medication with meperidine (Demerol) 75 mg., and scopolamine 0.4 mg., intramuscularly was given at 6:15 A.M. Immediate preanesthetic blood pressure in the left arm was 195/65, pulse 102, and respiration 20. Induction of anesthesia was accomplished with 400 mg. sodium thiopental (Pentothal) 2 per cent, preceded by dimethyl-tubocurarine

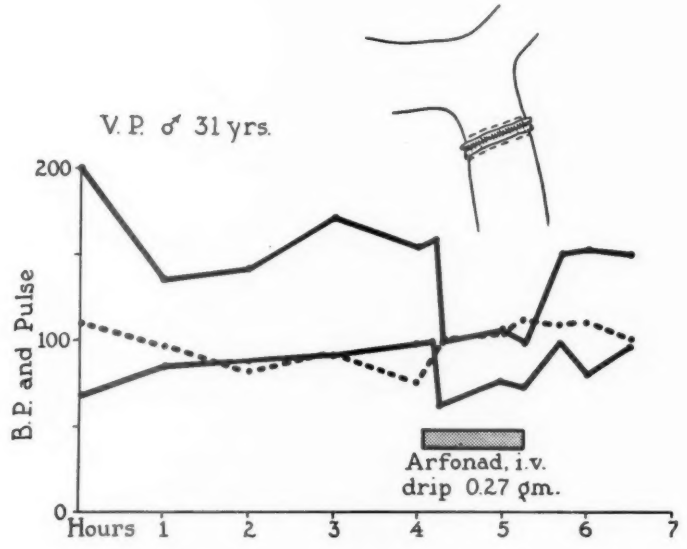

Fig. 1.—Blood pressure levels and pulse rates, period of Arfonad administration, and type of procedure in Case 1.

iodide (Metubine) 8 mg. Intratracheal anesthesia was maintained with cyclopropane and diethyl ether in a closed circle system. Ten minutes of apnea followed the administration of induction agents, and during that time respiration was carried out manually. Twelve minutes after the induction of anesthesia, the blood pressure had fallen to 160/70 in the arm, and the pulse was 90.

The patient was then turned on the right side. The operation started forty minutes after induction of anesthesia, at which time the blood pressure was 140/85, and the pulse rate 100, respiration 22. Blood transfusions were started simultaneously in each leg. The left fourth rib was removed subperiosteally and the third, fifth, and sixth ribs were divided at the angles. A coarctation of the usual type, plus a short patent ductus, was found. Respiration was assisted during the operation, and, just before the chest was opened, 4 mg. of additional dimethyl tubocurarine was given to facilitate assistance of respiration. The systolic blood pressure ranged from 140 to 170 mm. Hg, with little change in the diastolic readings and the pulse rate (Fig. 1). By the time the coarcted segment had been freed, 1,000 c.c. of blood had been given.

At this point, trimethaphan camphorsulfonate (Arfonad) was given in a concentration of 0.1 per cent by intravenous drip. There was a prompt fall in blood pressure to 105/70. The pulse rate rose to 100. Hypotension was maintained for seventy-five minutes while the friable ductus was divided and closed, the coarctation was resected, and the anastomosis was completed. Despite some bleeding from the friable ductus as it was being closed, the measured blood loss was 970 c.c. but 2,500 c.c. had been given by this time, an excessive amount as shown by studies of the peripheral blood during the following two days. Within ten minutes after the Arfonad infusion had been discontinued, the blood pressure in the arm rose to 150/90 and the pulse rate was 110, and thereafter remained unchanged until the anesthetic was discontinued. The anastomosis remained completely dry.

Throughout the entire anesthetic period the patient's color remained pink, the skin was dry and warm, and the capillary refill time was prompt. The patient answered questions within fifteen minutes after the anesthetic was discontinued. Three days later the arm pressures were 140/90. The recovery was completely uneventful; he was ambulant on the tenth day and was dismissed a week later. Currently the pressure in the upper extremities averages 146/66 while the systolic pressure in the legs is 136 mm. Hg, and all pulsations in the lower extremities are normal.

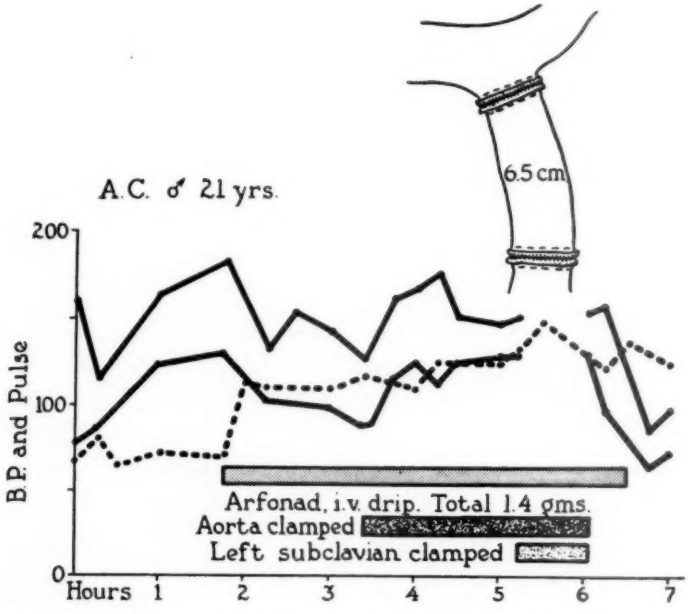

Fig. 2.—Blood pressure levels and pulse rates, periods of Arfonad administration, and vascular occlusion, and type of procedure in Case 2.

Case 2.—A. C., a 21-year-old man with hypertension, presumably the cause of his rejection for military service in 1952, also had diminished femoral pulses. The arm pressures were 158/78 and the systolic pressure in the legs was approximately 90 mm. Hg. There was marked acne over the chest and back, and pulsating vessels could be felt in the scapular areas. The chest x-ray examination showed indentation of the left border of the aorta above the pulmonary artery and notching of the third, fourth, fifth, sixth, seventh, and eighth ribs bilaterally. The cardiac shadow was normal. The electrocardiogram showed left ventricular hypertrophy. Operation was deferred pending improvement of the acne, and the coarctation was resected on June 9, 1954.

Preoperative medication with meperidine 50 mg. and scopolamine 0.4 mg. was given at 6:45 A.M. Preoperative blood pressure in the left arm was 165/75, pulse rate 78, respiration 20. Anesthesia was induced with 400 mg. sodium thiopental 2 per cent, preceded by

dimethyl-tubocurarine iodide 8 mg. There followed a period of apnea of about ten minutes' duration associated with a fall in blood pressure to 115/80 with a pulse rate of 86. Anesthesia was continued with intratracheal cyclopropane and diethyl ether in a closed system and, within thirty minutes, the pressure was 155/115 with a pulse rate of 70. Respiration was assisted throughout the operation. The left fifth rib was removed, and the third, fourth, fifth, and seventh ribs were divided at their angles. The intervening intercostal bundles were divided and ligated. The presence of a patent ductus, an 8 mm. aneurysm of the first left intercostal artery, and what appeared to be a large (6 mm.) bronchial artery, necessitated resection of a long segment, the use of an homologous graft and a long period of clamp application. Finally, it became apparent that only by clamping the aorta proximal to the subclavian artery could a safe anastomosis be made.

Early in the operative course the blood pressure rose steadily (Fig. 2) to 180/120 with little change in the pulse rate. At this point, a continuous infusion of 0.1 per cent trimethaphan camphorsulphonate (Arfonad) was started; this was followed by a steady decline of systolic blood pressure to 130 mm. Hg, over the next thirty minutes, the diastolic blood pressure averaging 100 mm. Hg. Within ten minutes of the start of the infusion, the pulse rate had risen from 82 to 116 per minute, and remained at this approximate level for the next one and one-half hours, during the last half hour of which time the systolic blood pressure in the left arm again began to rise to an average of 170 mm. Hg, with corresponding rise in diastolic pressure. This increase in systolic blood pressure began with the clamping of the aorta, and despite the increased rate of flow of Arfonad, it could not readily be corrected. Only after forty minutes was it possible to reduce systolic blood pressure.

While the clamp closed the aorta proximal to the subclavian artery, the pulse rate rose to a maximum of 148 per minute, and then gradually declined to 128, and it was soon noted that pulmonary edema began to develop. This was kept under partial control by use of positive pressure respiration during both inspiratory and expiratory phases, and immediately upon release of the clamps and re-establishment of general circulation, the patient was given lanatoside C (Cedilanid) 0.6 mg., intravenously. Within ten to fifteen minutes, all clinical signs of pulmonary edema had subsided, and the blood pressure now declined steadily over the next half hour to 85/60. The pulse rate, however, remained at an average of 130 per minute. Arfonad at this point was discontinued and the anesthesia was concluded with nitrous oxide-oxygen. Toward the end of the operation, there was a definite tendency for the blood pressure to rise and for the pulse rate to decline somewhat, so that the anesthesia was concluded with a blood pressure of 95/70, and a pulse rate of 120. The total anesthesia time was 6 hours, 55 minutes, and the patient was returned to his bed in reasonably good condition, but not yet reacting from anesthesia. The total amount of Arfonad used was 1.4 Gm., over a period of approximately five hours. Although there was no uncontrolled bleeding at any time, 2,500 c.c. of blood was used to replace the measured loss of 1,970 c.c., determined by weighing sponges and measuring the contents of the suction bottle.

The postoperative course was characterized by pulmonary edema and patchy atelectasis on the first day with a maximal temperature reading of 103° F. Jaundice appeared on the third postoperative day, the icteric index reaching 30 units, dropping to 18 units two days later, and subsiding completely thereafter. The urine was negative for hemoglobin and bilirubin. The patient made an otherwise uneventful recovery. When dismissed on the twentieth postoperative day the systolic pressure in the arms was 170 mm. Hg, and in the legs 190 mm. Hg. The current pressure in the arms is 124/70 and the systolic pressure in the legs is 120 mm. Hg, and pulsations are normal.

CASE 3.—W. M., a 28-year-old man, known to have a murmur since childhood, was rejected for military service in 1943 because of hypertension. His physician diagnosed coarctation of the aorta. Fatigue in the legs was the only complaint. The blood pressure in the arms was 180/90 and in the legs 120/80. Femoral pulses were diminished. Roentgenogram of the chest showed notching of the left border of the descending aorta, notching of the

third, fourth, fifth, sixth, seventh, and eighth ribs on the right, and fourth to ninth, inclusive, on the left. The cardiac shadow was normal. The electrocardiogram showed left ventricular hypertrophy and complete right bundle branch block. Aortic resection was performed on Oct. 20, 1954.

Preoperative medication, induction of anesthesia, intravenous therapy, and physical arrangements were along the lines described for the previous two cases. However, the management of Case 3 was changed from the others in that induction of anesthesia was preceded by the intravenous administration of chlorpromazine (Thorazine) 25 mg., in the hope that it might be possible to diminish the patient's requirements for general anesthesia which again was closed circle intratracheal cyclopropane and diethyl ether. It was also felt that it would be advantageous to begin the administration of Arfonad promptly after induction of anesthesia in order to minimize blood loss associated with the thoracotomy. This was done, and an excellent response to the continuous intravenous infusion of 0.1 per cent Arfonad was immediately obtained and maintained consistently (Fig. 3).

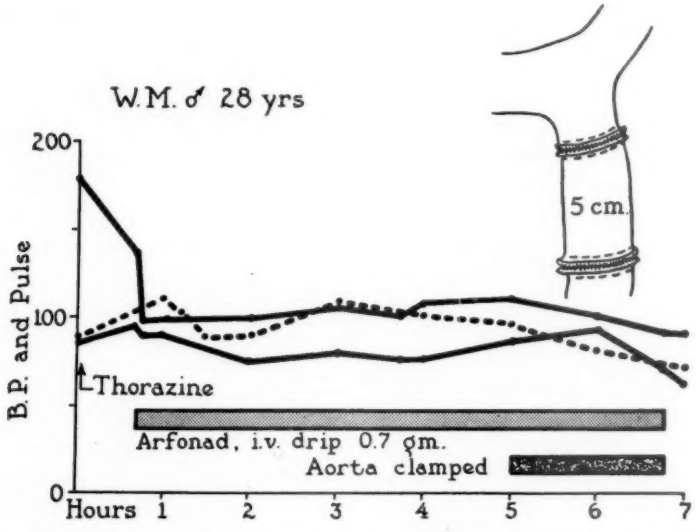

Fig. 3.—Blood pressure levels and pulse rates, periods of Arfonad administration, and aortic occlusion and type of procedure in Case 3.

The left fourth intercostal space was incised and division of the third, fourth, fifth, and sixth ribs at their angles was made. A graft 5 cm. in length was necessary because of the resection required to reach a suitable caliber of the aortic segments. A patent ductus arteriosus was present. Systolic blood pressure during the closure of the ductus, resection of the coaretation, and the installation of the graft remained at an average of 100 to 110 mm. Hg, and the diastolic at approximately 100 to 110 per minute, after a temporary initial rise to 140. There appeared to be no reason for decreasing the blood pressure further as the vessels were soft, permitting the vascular manipulations to be accomplished without difficulty. No significant change in blood pressure was noted during the clamping or release of the aorta. The measured blood loss was about 2,000 c.c. and a like amount was given. Only 700 mg. of Arfonad was required over a period of six hours, and the patient reacted promptly at the conclusion of anesthesia.

Recovery was completely uneventful. We were impressed by the good general condition following the long and extensive procedure, particularly the lack of anxiety and the minimal pain and discomfort. The pressure in the arms was 130/80 on the first postoperative day and remained essentially at that level, until dismissal on the seventeenth postoperative day. The arm pressures at present are 154/90 and the systolic pressure in the legs is 135 mm. Hg. The pulsations within the legs are normal.

DISCUSSION

The advantages of decreasing the pressure found normally or in pathologic states in the aorta or its major branches during operations upon them are at once obvious. It decreases the risk of hemorrhage and facilitates its control should it occur. With hypotension, vascular tears tend to remain localized instead of extending in all layers or producing a dissecting aneurysm as witnessed by Clagett and Jampolis[4] in one of their cases. Glenn and his associates[7] have called attention to the use of hypotension in dealing with patent ducti in adult patients. A decrease in the size of the vascular structures with thickening of their walls occurs as the pressure falls. Julian and associates[12] stated that lowering the pressure is a means of reducing trauma to a diseased aortic wall due to the pulse waves pounding the vascular wall against the occluding clamp. In addition to these mechanical advantages, induced hypotension has decreased operating time because of easier hemostasis in pelvic exenteration and in many neurosurgical procedures.[14]

The most serious complication in a patient surviving resection of an aortic segment is paralysis due to hypoxia of the spinal cord. Blalock and his associates[3] reported one instance of paralysis of the legs in a patient in whom the coarctation was by-passed by anastomosis of the subclavian artery to the aorta distal to the site of obstruction. The complication was ascribed to thrombosis of the anterior spinal artery. Gross[9] reported spinal cord damage in two adults, aged 31 and 50 years, following satisfactory excision of the coarctation. They survived the procedure but had serious neurological damage affecting both legs. Beattie and his associates[1] reported an instance of paralysis following surgical correction of a coarctation in a 29-year-old man during which the subclavian artery was occluded for thirty-eight minutes. Paralysis of both legs was present the next morning. Death occurred on the fifth postoperative day. Autopsy disclosed degenerative changes in the lower spinal cord and hemoglobinuric nephrosis; the latter is much more prone to occur in the presence of renal hypoxia from a degree of hemoglobinemia insufficient to harm normal kidneys.

The blood supply to the spinal cord is from the anterior spinal artery[1] which is formed by a junction of a branch from each vertebral artery, the vertebral arteries arising from the corresponding subclavian artery. In addition, anastomotic branches from the intercostal and lumbar arteries also join the anterior spinal artery. It seems unlikely that application of clamps to the aorta in coarctation would interfere with the blood supply through the lumbar and intercostal branches in the presence of the usual extensive collateral circulation. Even the division of the upper intercostal vessels should leave adequate collateral circulation. Clamping of the subclavian artery, however, might impair circulation through the anterior spinal artery as pointed out by Beattie in the discussion of his case. It was necessary in one of ours (Case 2) but was not followed by any neurological disturbance.

In their early experiments in aortic resection, Gross and Hufnagel[8] showed that the incidence of hind-quarter paralysis in dogs could be diminished fol-

lowing periods of aortic occlusion by packing the animal's back in ice. Beattie and his co-workers[2] showed that the thoracic aorta could be occluded for as long as ninety minutes in refrigerated dogs without developing spinal cord damage. Clinical application of hypothermia to protect the spinal cord from hypoxia during aortic occlusion has been described by Julian and his associates[11] and by DeBakey and Cooley.[6]

The hazards of lowering the blood pressure during the period of aortic clamping is obviously vastly different in patients undergoing surgery for coarctation than in those in whom thoracic aneurysms are to be resected. In the former instances, there is already an extensive collateral circulation and the application of clamps to the aorta makes little difference since little or no blood has been passing through the coarctation. The hypotension induced by blocking of autonomic ganglia is fundamentally different than the hypotension seen in loss of circulating blood volume, as in shock from trauma or hemorrhage. It brings about vasodilation with decrease in pressure without antecedent vasoconstriction which produces tissue hypoxia. Adequate cardiac output, capillary circulation, and venous return are maintained. If adequate oxygen tension is maintained in the blood, tissue hypoxia does not develop, and blood flow to vital organs is not significantly reduced.

Since controlled hypotension by ganglionic blockade is obtained through a process of vasodilation, it is important that the blood volume be as close to normal as possible before hypotension is induced. Therefore, it is logical that hypotension should be induced before any significant blood loss has actually occurred. In Case 1, it was felt that it might be too hazardous to subject the patient to prolonged hypotension, and, therefore, Arfonad was started only when it became important from a surgical point of view. It is for this reason that we wished to avoid any deficit in circulating blood volume, and, in so doing, we transfused more blood than was required. Additional experience gained with prolonged hypotension in the intervening period suggested the use of hypotension from the beginning in Case 3, and this was found to be quite safe and most satisfactory. It should also be noted that no effort was made to reduce blood pressure to any preconceived level. We were guided entirely by the adequacy, or otherwise, of the operating conditions. It appears that more important than the actual level of blood pressure is the diminution of pulse pressure, and this was obtained in all cases, despite the fact that the reduction of systolic pressure in Case 2 was small and inconstant.

The occurrence of pulmonary edema in Case 2 is interesting. Hypotension through vasodilation so reduces peripheral resistance that despite a somewhat diminished venous return and reduced cardiac output, the over-all workload of the heart is significantly lessened. Thus, it has been possible to use Arfonad in the treatment of pulmonary edema of cardiac origin.[15] While the blood flow through the aorta is completely abolished by the application of clamps, the degree of benefit derived from the diminished peripheral resistance will depend upon the proportion of systemic circulation to the lower part of the body maintained through the collateral bed. The narrower the existing

channel in the coarcted segment, the less significant, from a circulatory point of view, becomes the application of clamps. However, as soon as an additional significant portion of the unoccluded vascular bed had been sequestered by a clamp applied proximal to the left subclavian artery, as in Case 2, and the total available circulating bed had thus been further restricted, the left heart became unable to dispose of its venous return with consequent back pressure into the pulmonary circulation and the development of pulmonary edema. For this reason, the removal of the clamps and rapid partial digitalization was followed by prompt return to normal, although crepitant rales could still be detected during the next forty-eight hours; the temporary exacerbation of pulmonary edema postoperatively is explained by the damage to lung capillaries incurred during the initial episode. The occurrence of pulmonary edema during the operation caused great anxiety, especially as there was no immediate remedy available as long as the clamp occluded the aorta proximal to the left subclavian artery. By means of positive pressure ventilation, however, it was possible to tide the patient over this critical period.

SUMMARY AND CONCLUSIONS

Three cases of resection of coarctation of the aorta in adults are reported and the experiences with this operation under controlled hypotension with Arfonad are discussed.

It is felt that controlled hypotension for this type of operation is of decided advantage in that it renders the actual surgical dissection and anastomosis less hazardous and easier to accomplish. Also, when the clamps have been removed, it is possible to test the line of anastomosis under conditions of diminished intravascular pressure, and thus to close any leaks without significant loss of blood and obscuring the surgical field. As the pressure is allowed to rise slowly, the anastomosis is exposed to the increased impact in a gradual manner, instead of being suddenly distended by blood under normal pressure.

The reduction of peripheral resistance markedly diminishes the chances of untoward repercussions on the lesser circulation while the clamps are in position, although there are definite limitations to this, as was demonstrated in one of the cases. In the light of our experience, it has proved not only feasible, but also advantageous, to induce hypotension as soon as the operation is begun, thereby diminishing the cumulative blood loss associated with a prolonged procedure in a field rich in greatly enlarged anastomotic channels.

The criterion as to the exact degree of hypotension for each case should be the surgical requirements, and blood pressure is always maintained at the highest level compatible with these needs. It is felt that in resection of a coarctation, hypothermia has probably little to offer as far as additional safety for the patient is concerned, unless there is evidence of inadequate collateral circulation. On the other hand, hypothermia would be obligatory where resection of the thoracic aorta was carried out for aneurysm, in order to protect the spinal cord from hypoxic damage in the absence of a well-developed collateral circulation.

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SUCCESSFUL SURGICAL EXTIRPATION OF GIGANTIC CONGENITAL CYSTIC HYGROMA

Case Report

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CYSTIC hygroma is a multilocular, thin-walled, endothelium-lined tumor of lymphatic origin, containing thin, serous, colorless fluid, unless there has been a superimposed hemorrhage staining it xanthochromatic or bloody.

The lesion is congenital in origin. Gross,[8] in his large series of 112 cases, reported 65 per cent noted at birth, 80 per cent discovered within the first year, and 90 per cent present by the end of the second year. It has been rarely reported appearing in adult life.[16, 20]

Goetsch[6] indicated that these tumors originate from a sequestration of primitive lymphatic sacs lacking the usual communicative channels with the venous system and preserving their independent power of growth and their ability to secrete lymph.[9, 10, 15] Although they are classified as benign tumors, due to their great tendency to invade deeper structures along large vessels, nerves, and fascial planes, many have considered them of a malignant nature. They are most frequently encountered in the posterior triangle of the neck and occasionally invade the floor of the mouth, tongue,[17] parotid region, and mediastinum.[7, 8] They have been reported also in the axilla and groin.[8, 9]

Extensive reviews of the etiology, pathology, incidence, and diagnosis have recently been made by Gross[8] and Ward and associates[20] and will not be repeated here. The purpose of this paper is to report the successful surgical removal of a gigantic cystic hygroma and to review briefly the present methods of management. The lesion involved the entire right side of the neck and axilla and was the cause of an obstructive dystocia during labor, necessitating a cesarean section.

CASE REPORT

This infant was a full-term girl, born to a young mother on Oct. 13, 1953, by cesarean section because of an obstructive dystocia caused by a large tumor mass in the right side of the neck. It is of interest that roentgen pelvimetry studies performed on the mother because of the absence of progress during the first eight hours of labor, revealed that "a large soft tissue mass could be seen on the right side of the baby's neck between the head and the right shoulder. The mass displaced the right shoulder outward and caudally."

Physical examination revealed a well-developed, 9-pound, normal infant, except for a massive cystic tumor which filled the right lateral hollow of the neck and extended posteriorly over the entire scapula. A second mass, smaller in size, was noted in the right axillary

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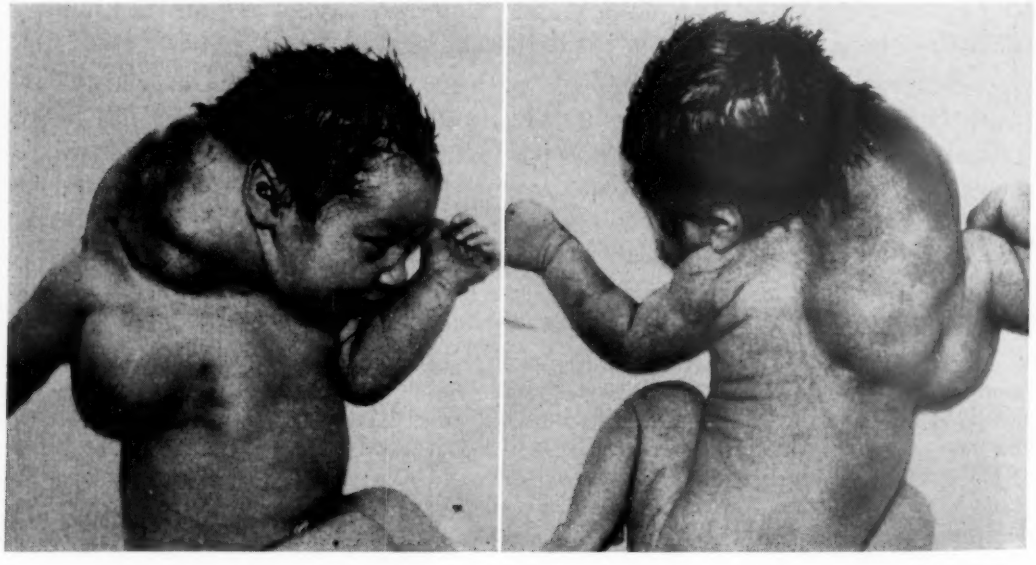
region. These two masses appeared to communicate behind the clavical and under the arm. The overlying skin was under marked tension, very thin, and with a slightly bluish cast imparted to it by the underlying hemorrhagic cysts. In other areas the skin was of a pinkish color, and the softer, compressible cystic masses could be transilluminated.

Fig. 1.—Roentgen pelvimetric studies performed on the mother show a large soft tissue mass on the right side of the infant's neck between the head and the right shoulder, causing an obstructive dystocia.

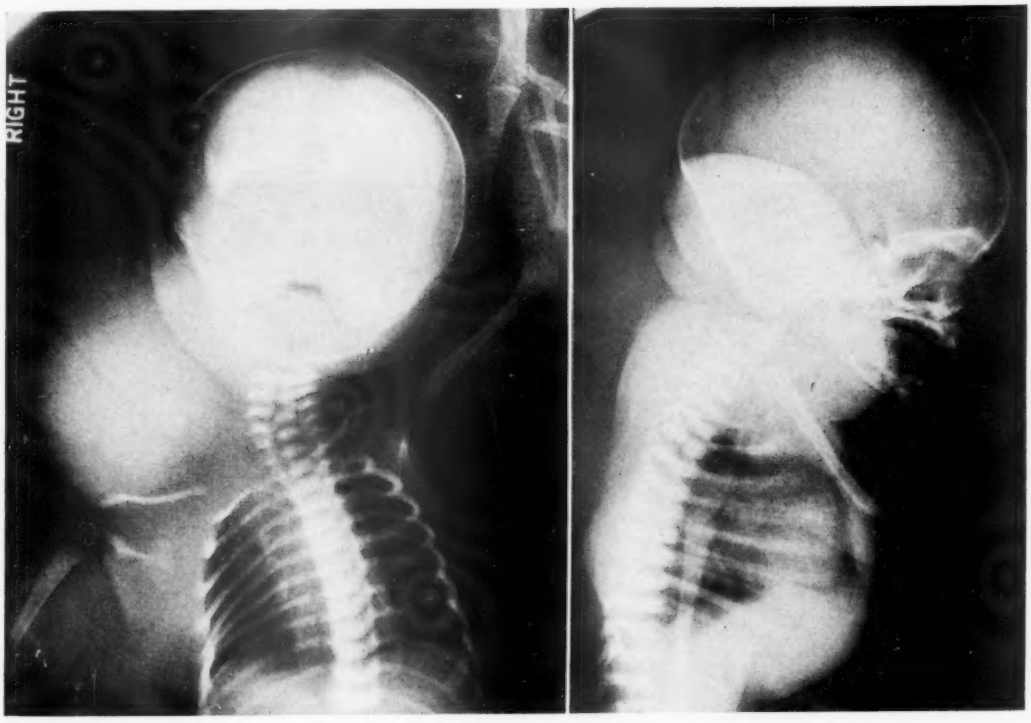


A. *B.*

Fig. 2.—*A* and *B*, Photographs of the infant at birth, show a gigantic cystic hygroma of the neck, scapular, and axillary regions.

Roentgen examination revealed a very large soft tissue tumor mass occupying the right side of the neck and the entire scapula, supraclavicular, and axillary regions. The shoulder girdle was markedly displaced laterally. The upper cervical spine and head were displaced to the normal side. The mediastinum and chest appeared normal.

The diagnosis of cystic hygroma was made and surgical excision in two stages was advised to be carried out as early as possible, since hemorrhage, infection, and ulceration of the thin, tense skin, or increase in the size of the tumor with invasion of other vital structures, would further endanger the child's life and also make the surgical procedure technically more difficult.



A. *B.*

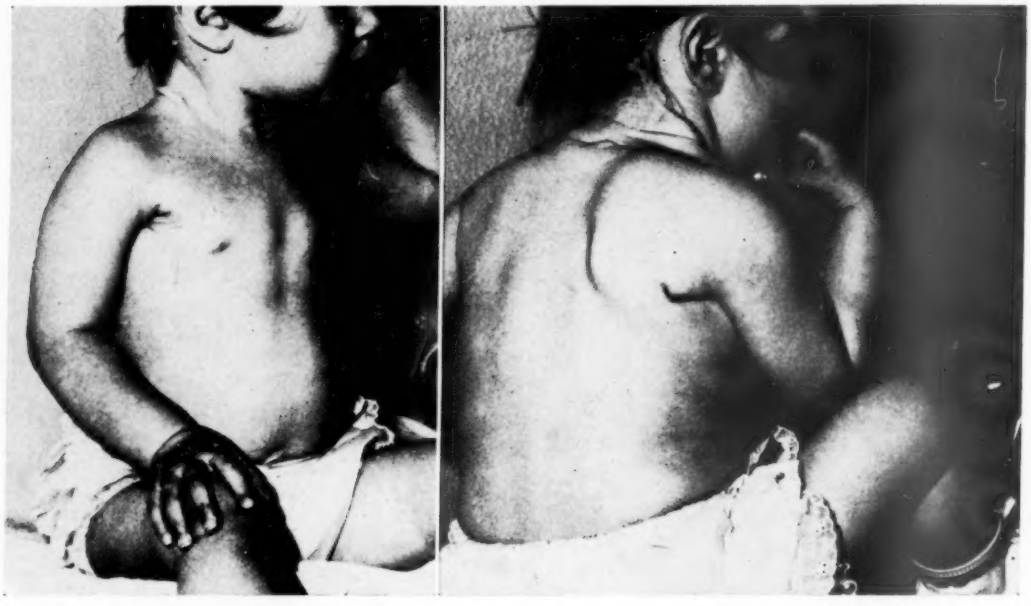
Fig. 3.—*A* and *B*, Roentgenograms of the infant at birth, reveal a very large tumor mass occupying the right side of the neck and entire scapular, supraclavicular, and axillary regions. The shoulder girdle is markedly displaced laterally. The upper cervical spine and head are displaced to the normal side. The mediastinum and chest appear normal.

Accordingly, two days after birth, the infant was operated upon under intratracheal anesthesia. An anteroposterior elliptical incision was made over the presenting mass in the neck. A large, irregular, thin-walled, multiloculated cystic mass was identified. Anteriorly, the tumor extended behind the clavicle and communicated with the axillary mass; between cysts the brachial plexus, phrenic nerve, and subclavian and axillary vessels were identified. Posteriorly, the scapula appeared embedded in tumor tissue; the rhomboid, serratus anterior, trapezius, and sternocleidomastoid muscles were almost completely destroyed; only thin muscle bundles could be identified. The spinal accessory nerve was not identified. Medially, the carotid artery and internal jugular vein were also identified and preserved.

After slow, tedious dissection, all the vital structures were isolated and protected from injury and the entire mass was removed, with the exception of that portion situated below the clavicle and in the axilla. The reconstruction was found to be very difficult because all the fascial planes and muscles had been virtually destroyed by the tumor. The scapula was fixed by suturing the vertebral edge to the long spinal muscles. A few interrupted

sutures were placed between the remnants of the trapezius muscle and the spine of the scapula. Three rubber drains were left in place. The platysma muscle and skin edges were approximated separately by interrupted sutures. The right arm was immobilized for forty-eight hours; thereafter, a small dressing was placed over the wound and active motion was allowed. Postoperatively, there was a moderate degree of muscle weakness of the right arm, but the brachial plexus appeared to be intact. On the fifth postoperative day, the rubber drains were removed and the wound healed without fluid collection.

Sixteen days after the first operation, resection of the axillary portion of the tumor was undertaken. A transverse incision was made over the most prominent part of the tumor. A multiloculated cystic tumor which occupied the entire axilla, subpectoral, and subscapular spaces, was identified. At this operation a large amount of fibrous tissue around the brachial plexus and axillary vessels was encountered. For this reason, the tumor had to be removed by sharp dissection almost in its entirety. Considerable bleeding accompanied this maneuver, but adequate blood replacement was carried out. The long thoracic nerve was not identified. The wound was closed by interrupted sutures after placing two rubber drains in the axillary



A. *B.*

Fig. 4.—*A* and *B*, Photographs of the infant sixteen months after surgical removal of the tumor, show excellent functional and cosmetic results. There are no signs of tumor recurrence.

and subscapular regions. Postoperatively, the infant made an uneventful recovery and was discharged three weeks following the second operation, with a well-healed scar and with moderate muscle weakness of the right arm. Again there were no signs of brachial plexus injury.

At present, two years after the operation, there are no signs of tumor recurrence and there is no appreciable weakness of the right arm. The cosmetic and functional results are considered excellent with the exception of a winged scapula.

METHODS OF TREATMENT AND DISCUSSION

Many forms of treatment have been suggested over a period of years, namely, expectant treatment, aspiration and injection of sclerosing solutions, radium and roentgen irradiation, and, finally, surgical excision. Expectant

treatment was first recommended by Fraser,[4] and it consisted of waiting for an indefinite period of time for the cystic hygroma to undergo spontaneous regression. Since the likelihood of this course of events is small, and because of the danger of rapid growth, invasion of vital structures, and infection, a more aggressive attitude is indicated. Gross[7] reported two cases in which suppuration occurred in a hygroma following a tonsillitis and upper respiratory infection, which required incision and drainage of the cystic tumor with apparent definite cure.

Aspiration with subsequent injection of sclerosing solutions (25 per cent glucose, 25 per cent sodium morrhuate) has been carried out by many physicians. It is now generally agreed that simple aspiration does not offer a permanent cure, and there is a large risk of secondary infection, or even a fatal complication. Ward and associates[20] recommended the use of this method of treatment in preparation for surgical excision in three to six weeks. On the other hand, Gross,[7] Sawyer and Woodruff,[18] and others subscribed to the idea of early surgical treatment. We wish to stress the latter point. In our limited experience of three cases, the surgical removal of the tumor was much simpler when the patient was operated upon shortly after the discovery of the tumor. Aspiration with subsequent injection of sclerosing solution should be reserved for the remnants remaining after surgery.[8] Aspiration alone is indicated only as an emergency procedure for decompression purposes, as in the rare case of marked displacement of the larynx or compression of the great vessels.

Radium and roentgen-ray irradiation therapy fell in disrepute following the report of Figi,[3] in 1929. In his series of twelve cases treated by radium therapy, seven patients died of sepsis. Of the remaining five patients, three were completely cured and two were much improved. However, with the advent of chemotherapy and antibiotics, sepsis does not appear to be a problem any longer. Martin,[11] Pfahler,[12] and Portman[13] recently reported a number of patients who have been successfully treated with x-ray therapy or radium. Martin[11] has reported the single largest series of cases treated in this manner. It is of interest that all of these patients presented rather small tumor masses with no mediastinal extension. Two of the nine patients reported by Martin[11] were classified as failures. Of the remaining seven, three required plastic surgery at a later date. He also reported one case without evidence of tumor recurrence sixteen years after receiving 2,000 r (air) roentgen therapy, which had exhibited evidence of retarded development of the right shoulder girdle and breast. The major disadvantage of this form of treatment is that response is relatively slow and the treatment has to be extended over a period of months, necessitating an average high total dosage ranging between 3,000 and 5,000 r for its cure. Throughout the literature we have found many reports of radioresistant cystic hygromas.[5, 7, 17, 19] Theoretically, there is also the drawback of the effect of radiation on the growth centers. Although we did not find any case in the literature of cystic hygroma with growth irregularity following such treatments, this has always concerned us. We believe that there is a place for x-ray therapy in those tumors invading widely the musculature of the tongue, floor of the mouth, and cheek, in which surgery would prove to be a mutilating

procedure. Singleton[19] and Goetsch[6] reported favorable results wherein excision of the cervical portion of the tumor was followed by postoperative x-ray therapy to the mediastinum.

Surgical excision is the treatment of choice in the majority of cases. Years ago, before the antibiotic days, the surgical mortality was rather high. At present, due to the advances in anesthesia and improvement in surgical techniques, early surgical excision of these tumors has proved to be associated with a very low mortality. The largest surgical series reported is that of Gross.[7] He reported 112 patients operated upon in one or more stages with only six deaths. Frequently, multiple surgical procedures will be necessary because of the size of the tumor, weakened condition of the patient, or recurrences of the tumor. Recurrences usually appear within a year following the operation.[20] Recently, Ravitch[14] reported two cases of very extensive cystic hygromas successfully treated by a forequarter amputation and hemipelvectomy. This radical surgical procedure, although mandatory occasionally, usually can be avoided as a primary form of treatment. It has been our experience that even though the tumor may appear clinically gigantic and invasive, at surgery the simple, careful dissection and protection of the large vessels, nerves, and vital structures, followed by the approximation of the remnants of fascia and muscle bundles, will later prove a surprising, gratifying functional and cosmetic result.

CONCLUSION

A gigantic cystic hygroma of the neck and axilla, successfully operated upon on the second day of birth with excellent functional and cosmetic results, is reported. The various forms of treatment suggested for this condition have been reviewed. Aspiration, followed by subsequent injection of sclerosing agents should only be used for the remnants remaining after surgery. Radium and roentgen therapy are the treatments of choice in those tumors invading widely the musculature of the tongue, floor of the mouth, and cheek in which surgery would prove to be a mutilating procedure. Surgical excision is the treatment of choice in the majority of cases. The early surgical removal of the tumor has been stressed. Radical surgical treatment of the forequarter amputation type should not be undertaken as a primary form of treatment.

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RUPTURE OF THE HEPATIC DUCTS DUE TO BLUNT TRAUMA

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INTRODUCTION

MASON, Sidbury, and Guiang[2] have recently reviewed the literature on rupture of the extrahepatic ducts from nonpenetrating trauma and have added one definite and another probable case. They estimate that less than 100 cases have been reported in the last century. Certainly reports within the last ten years have been few and most of these have dealt with children, although, in 1938, Lewis[1] reported a case in an adult and summarized three others from the literature. The following is the report of an instance of rupture of the right and left hepatic ducts at the porta hepatis due to blunt trauma.

CASE REPORT

W. W., a 34-year-old Negro man, was admitted to the emergency division of Rochester Municipal Hospital on Aug. 21, 1954. He had been in an automobile accident approximately one hour prior to admission and on arrival had already received morphine 14 mg. Physical examination indicated that the patient was lethargic, had an alcoholic odor to his breath, and was only partially oriented. He had a forehead contusion, missing teeth, and a facial laceration. Tenderness was present over both costal margins laterally. Inconstant abdominal and right flank tenderness and guarding were present. Bowel sounds were absent.

Four hours following admission, the patient voided grossly bloody urine and complained of bilateral costovertebral angle tenderness. Shortly thereafter he developed a painful cough productive of sputum streaked with bright red blood. The abdomen remained flat and slightly tense with guarding that was greater on the right than on the left. An intravenous pyelogram was suggestive of bilateral subcapsular renal hemorrhage or rupture of the kidneys.

During the next forty-eight hours the patient received supportive care and improved symptomatically. His urine cleared, bowel sounds returned, and he had a normal bowel movement. Residual signs included a moderately distended abdomen with diffuse mild tenderness and guarding. Vital signs remained stable. A diagnostic paracentesis yielded bile. Eighty-four hours after admission the patient was taken to the operating room, and a right upper abdominal paramedian incision was made. The peritoneal cavity contained approximately 1,500 ml. of green-yellow bile and the viscera were stained yellow. Two small serosal tears were present in the duodenum. Inflammatory reaction was minimal. The gall bladder was red and thick-walled, but no stones were palpable. On careful exploration the only source of bile leakage was found to be from a small transverse laceration of the porta hepatis that partially divided both the right and the left hepatic ducts. At this time the patient had been under anesthesia for a period of four hours and his condition had gradually deteriorated to the point that he was dangerously hypotensive. The anesthetist urgently requested that the operation be terminated and, accordingly, a cholangiogram was not obtained. A large catheter was placed in the gall bladder and two cigarette drains were placed in the region of Morrison's pouch. Postoperatively the course was smooth except for minor atelec-

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tasis. Drainage from the gall bladder catheter was scant. Discharge around the drains, at first copious, gradually subsided so that the second drain could be removed on the ninth postoperative day.

The icterus index and alkaline phosphatase gradually fell toward normal values. Cholangiograms were obtained on the sixth and eighth postoperative days by injecting dye through the gall bladder catheter. Dye extravasation (Fig. 1) could be seen in the region of the porta hepatis. An intravenous cholangiogram made on the twenty-second postoperative day showed a normal duct system.

Fig. 1.—A cholangiogram made through the gall bladder catheter on the seventh postoperative day shows dye extravasation in the region of the porta hepatis. The second catheter replaced one of the cigarette drains.

DISCUSSION

Not often does blunt trauma cause rupture of an intra-abdominal viscus, and very rarely does it result in injury to the extrahepatic biliary system. The mechanism of such an injury is uncertain and there is no good explanation as to what circumstances contribute to rupture of the ducts.

Initially, this patient was thought to have had a brain concussion and to have contusion of the kidneys. The abdominal signs were ascribed to a reflex

adynamic ileus. As in the reported cases, the diagnosis in this patient was made rather late and then only with the aid of diagnostic paracentesis. Since, initially, sterile bile causes only minimal peritoneal reaction, it is not surprising that in the absence of other major intra-abdominal injury abdominal signs were not striking.

Once the diagnosis has been made, and in the absence of other more serious injuries, it is logical that the patient should be explored as soon as his general condition permits. Generally speaking, the longer the delay in diagnosis, the longer it will take to ready the patient for operation. The operative repair will depend on the type of duct injury and the general condition of the patient. It is felt that if the injury is not easily identified immediately, an operative cholangiogram will help to locate it and conserve valuable time. Such a cholangiogram can be made in a variety of ways, perhaps the most simple being the injection of dye directly into the common duct using a small hypodermic needle attached to a syringe. This method has been used satisfactorily in a patient suspected of having biliary atresia and in another with sclerosing cholangitis.

SUMMARY

A case of rupture of the hepatic ducts at the porta hepatis due to blunt trauma in an adult Negro man is reported. Diagnostic paracentesis was helpful in establishing the diagnosis. It is suggested that operative cholangiograms would be helpful in locating the site of injury to the duct.

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XANTHOMATOSIS OF THE STOMACH

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LIPOID-LADEN cells are observed in xanthoses of the skin. Similar cells are components of neoplasms that occur in connection with tendon sheets. Infiltration of viscera and lymph nodes by similar cells has been observed in patients with hypercholesterolemia due to obstruction of the common bile duct.[5] Xanthomatosis of the stomach was reported first by Loi in 1935.[6] Circumscribed xanthomata of the stomach were observed at necropsy by Bartolini[1] in 16 patients. Subsequently xanthomatosis of the stomach was recorded by Cazal,[3] Dubost,[4] Baumel,[2] and Umbach.[7] In all these instances, no hypercholesterolemia was reported, nor were similar lesions observed elsewhere than in the stomach. This paper records xanthomatosis of the stomach treated by gastric resection, the diagnosis having been made by frozen section during operation.

CASE REPORT

Clinical History.—O. H., a 38-year-old white man, was admitted to the Veterans Administration Hospital, Houston, Texas, July 6, 1954, with intermittent epigastric pain. He first had pain in the abdomen in 1942, while in the Navy. At that time an exploratory laparotomy was performed. Since then, he received an ulcer diet and antacids. The patient continued to have episodes of abdominal pain. Roentgenograms in 1945 revealed deformity of the duodenal bulb. In June, 1954, he was admitted to a hospital in Paducah, Kentucky, with severe exacerbation of previous symptoms and, without roentgenologic examination, he was placed on a more strict diet and was discharged June 30. Two weeks later nausea and vomiting occurred in addition to the other symptoms and he was admitted to this hospital.

At this time the patient was well developed, thin, and appeared chronically ill. The temperature was 103.4° F., the pulse rate 80, and the blood pressure 125 systolic and 80 diastolic. The abdomen was tender on the right, especially in the lower quadrant. The hepatic area was painful on percussion.

Urinalysis gave essentially negative results. The erythrocyte count was 6,220,000; the hemoglobin content 19.2 Gm. The thymol turbidity test was 4 units; the alkaline phosphatase 6.5 Bodansky units; the Bromsulphalein retention was 11 per cent in forty-five minutes. The gastric content contained 25 meq. per liter of free HCl. The Kahn test of the blood was negative. Roentgenographic examinations of the chest and of the gall bladder were negative. The stomach was of usual size with persistent spasm in the antral region suggestive of gastritis. The duodenal bulb could not be visualized clearly.

A clinical diagnosis of penetrating peptic ulcer was inferred. The patient was given atropine, penicillin, and streptomycin, and his condition improved. On August 17, the erythrocyte count was 5,120,000; the hemoglobin content 14.9 Gm. The white blood cell count was 8,250 with neutrophils 65, stabs 2, lymphocytes 27, monocytes 2, eosinophils 3, and basophils 1 per cent. At laparotomy August 26, the greater omentum was adherent to the

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anterior wall of the stomach. A subtotal gastrectomy with gastroduodenostomy was performed. During the procedure the splenic capsule was torn and the spleen was removed. A frozen-section diagnosis of xanthomatosis of the stomach was made. Three days following operation, urinalysis gave negative results; the hemoglobin content of the blood was 13.3 Gm.; the hematocrit 37 per cent; the total blood protein 5.4 Gm. per cent with albumin 3.8 Gm. and globulin 1.6 Gm. per cent. On September 6, the total cholesterol content of the blood was 220 mg. per cent. The patient was discharged September 11. When seen April, 1955, he was free of symptoms.

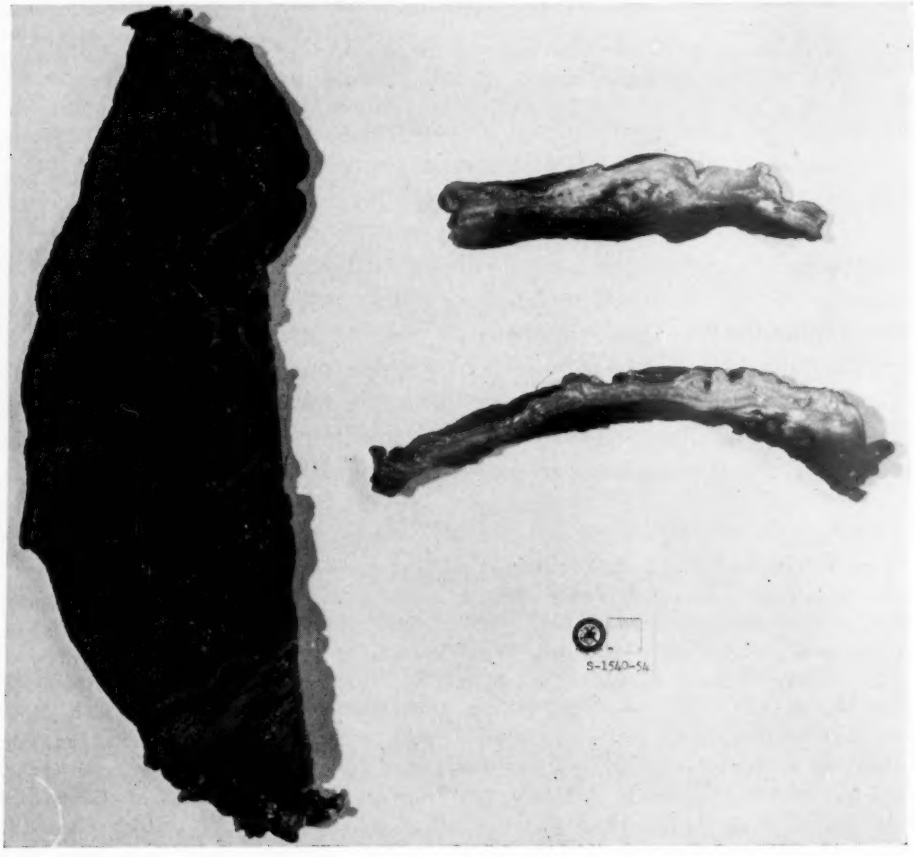

Fig. 1.—Specimen from xanthomatosis of the stomach in a 38-year-old white man. Nodular areas interrupt the muscular coat and protrude on the serosal surface. The rugal pattern of the mucosa is undisturbed.

The specimen consisted of the resected portion of stomach and the spleen. The stomach was opened along the greater curvature and measured 25 by 16 cm. A portion of greater omentum 26 by 8 cm. was attached. The rugae were prominent. There were no areas of ulceration or discoloration on the mucosal surface. On the serosa near the middle of the lesser curvature were several nodular masses, the largest 2 by 1.5 cm. The cut surfaces of these were bright yellow and lobulated (Fig. 1). They extended into and seemed to infiltrate the muscle coats. The spleen was 13 by 11 by 6 cm. and weighed 275 grams. The capsule was partly torn about the upper and lower poles. Cut surfaces were deep red with malpighian corpuscles discernible. Near the hilum over an area 2.5 by 1.5 cm., the capsule was raised and clotted blood filled the space beneath the capsule. Microscopic examination of the nodular areas and of other portions of the stomach disclosed sheets of large cells with foamy cytoplasm and small eccentrically placed nuclei. These lipoid-laden cells were in a scanty connective tissue stroma containing capillaries (Fig. 2). The cells infiltrating the

muscle bundles here and there completely erased the muscular pattern (Fig. 3). The surface epithelium appeared intact, as did the tunica propria, muscularis mucosae, and submucosa. Near the involved areas there was an increase in the connective tissue spreading apart the muscle bundles. There was also an increase in the connective tissue about blood vessels and nerves. In occasional areas giant cells resembling Touton cells were noted with many nuclei in the center of the cytoplasm and with vacuoles. Areas of necrosis were inconspicuous. Surrounding the involved fields there were dense infiltrations with eosinophilic granulocytes.

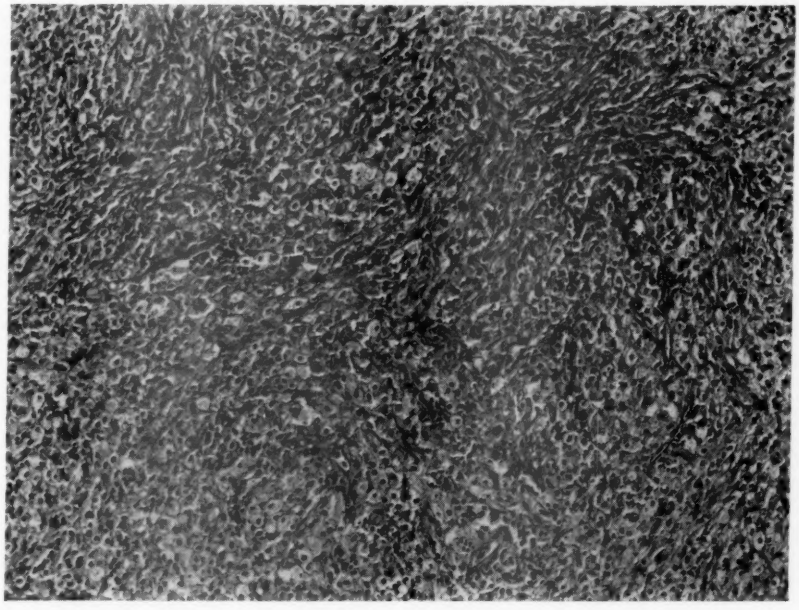

Fig. 2.—Photomicrograph of xanthomatosis of the stomach. Large cells with clear foamy cytoplasm cover the entire field (×100).

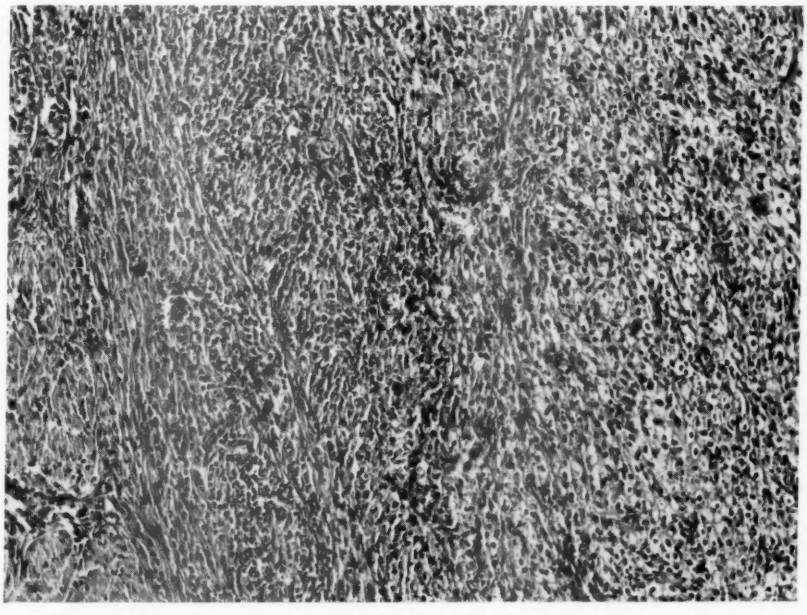

Fig. 3.—Photomicrograph of xanthomatosis of the stomach. In the periphery of the lesion foam cells infiltrate smooth muscle bundles (×100).

These were absent in the involved areas themselves. The lipid nature of the cells contained in the involved areas was demonstrated on frozen sections stained with sudan III, sudan IV, sudan black, and nile blue stains. In sudan III preparations, the cytoplasm of the foam cells stained pale orange with anisotropic foci discernible through polarized light. In sudan IV preparations, the content of the foam cells stained pale red and anisotropic foci appeared when viewed through polarized light. In sudan black preparations, the cytoplasm was pale blue with anisotropic foci less numerous. In nile blue preparations, the cytoplasm was pale pink with no anisotropic foci evident. In the regional lymph nodes examined, no lipoid-laden cells were noted. In the spleen the pattern was preserved with no lipid-containing cells present.

COMMENT

Xanthomatosis of the stomach appears to be an entity for which no characteristic clinical criteria have been evolved. The essential feature seems to be autonomous multicentric proliferation of lipoid-laden cells. They infiltrate and replace extensive areas of the muscular coat of the stomach wall. There was a concomitant increase in the connective tissue stroma between muscle bundles and around blood vessels and nerves. Dense infiltration with eosinophilic granulocytes was evident near and about the lesion but not in the lesion itself. No aggregations of lipoid-laden cells were seen either in the regional lymph nodes or in the spleen. Apparently, the lesion involving only the stomach is not a manifestation of a systemic disturbance of lipoid metabolism but is rather a local and probably neoplastic process.

SUMMARY

Xanthomatosis of the stomach is recorded in a 38-year-old white man who presented clinical signs and symptoms suggestive of gastric ulcer. Operative removal disclosed multiple focal lesions invading and replacing the muscular layers of the gastric wall. The patient has been free of symptoms for seven months following operation. This is believed to be the first recorded instance of xanthomatosis of the stomach treated by gastrectomy.

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GRANULOMATA CAUSED BY ABSORBABLE STARCH GLOVE POWDER

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THE prevalence of foreign body granulomata due to the use of talc as a lubricant for surgical gloves and the alarming numbers of patients with resulting adhesions led to much investigative work for an absorbable, non-irritating powder. Experiments with an epichlorhydrin-treated cornstarch were reported in 1947 by Lee and Lehman[1, 3] to be highly favorable, when compared with talc. (The epichlorhydrin application prevented any gelatinization during autoclaving.) This powder is known commercially as "BIO-SORB"* and appears as rounded or hexagonal acidophilic bodies 10 to 20 microns in diameter and with dark, often prominent, central dots. They respond to the periodic acid-Schiff's reagent staining technique and are anisotropic (Figs. 1 and 2). These workers found this material to be completely absorbed in three weeks from the peritoneum in ten dogs without any demonstrable inflammatory reaction when 1 Gm.-amounts—equivalent to the washings from 8 pairs of gloves—were employed. These initial findings were soon confirmed by others.[5]

From the beginning, however, it has been stressed that absorbable starch powder is not completely harmless and that reasonable precaution against gross contamination of a wound must be taken. Millimeter-sized yellow nodules were found scattered over the peritoneal surfaces of two of twelve dogs when 1 Gm.-amounts were used (compared with all of twelve other dogs having massive foreign body response to talc),[5] and this substance was reported occasionally to have given rise to granulomata at a distance from the site of implantation, with even the formation of adhesions.[2] Seelig[7] was concerned because BIO-SORB contains 2 per cent magnesium oxide for freer flow to prevent clumping of the powder. He had previously found that magnesium oxide in itself gives rise to foreign body granulomata and spoke against its inclusion in this glove powder; Postlethwait and associates,[6] on the other hand, did not think that the 2 per cent concentration of magnesium oxide was sufficient to be the causative agent. In an excellent article offered as a re-evaluation of the use of absorbable starch powder, Lee and co-workers[4] warned that although this starch powder has proved to be vastly superior to talc, to the extent that it had replaced the latter in 60 to 90 per cent of the hospitals in the United States by 1952, it would be foolish to lose sight of the limitations of this useful agent. The two principal points to be emphasized are: (1) although absorbable, until absorption takes place, the starch

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*Starch No. 108, Ethicon Suture Laboratories, Inc., New Brunswick, N. J.

granules constitute as much of a foreign body as would any other powder of comparable size; and (2) the completeness of absorption and the time necessary for its accomplishment is dependent upon the presence or absence of all factors conducive to inflammatory reaction. One of these controllable variables is complete dispersion of the powder, for, when adhesions occurred, they seemed to do so as the result of "clumps" of the powder which defy complete absorption for some time. "The longer absorption is delayed, the greater is the likelihood that the foreign-body reaction will be irreversible and that the adhesions will be permanent."

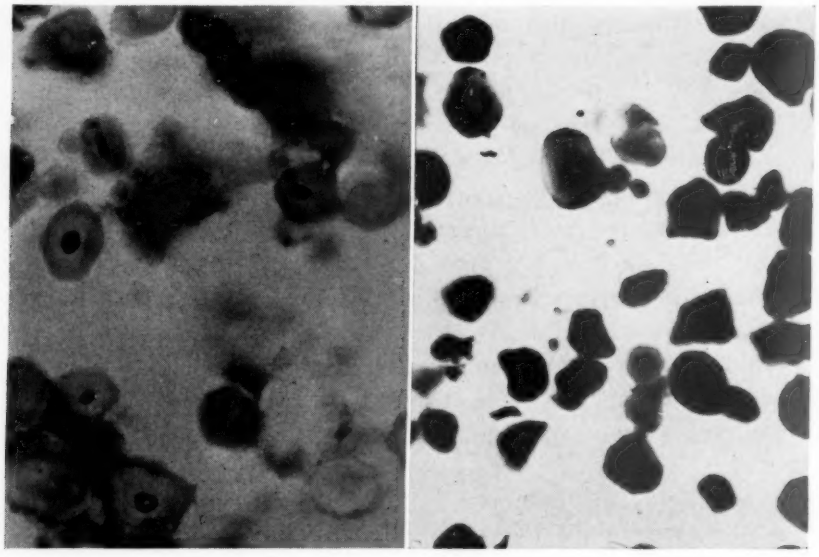

Fig. 1. Fig. 2.

Figs. 1 and 2.—Starch powder suspended in serum and processed as a cell block. Hematoxylin and eosin (H & E), and periodic acid-Schiff staining technique (PAS) (×770).

In the past several years, at the Hartford Hospital, there have been many instances of surgical specimens containing granules of absorbable starch powder on their surfaces coincident with their operative removal. In addition, there have been three cases since 1953 (two of them within the past four months) in which patients reoperated upon after intervals of 31, 37, and 79 days have developed foreign body granulomatous response to starch glove powder with varying degrees of intensity.

CASE 1.—E. B., a 27-year-old white woman, was first admitted to Hartford Hospital on July 7, 1953, with acute upper abdominal pain and vomiting. She was a gravida ii, para i with the expected due date of confinement September 27. The patient did well on conservative management. Oral cholecystogram revealed a nonfunctioning gall bladder. The patient was discharged after eleven days in the hospital.

She was readmitted on September 12 for an elective cesarean section; her first pregnancy terminated in a stillbirth after a difficult labor, and she was now found to have a pelvic disproportion. A low-flap cesarean section was performed on September 14. After removal of the infant and placenta without difficulty, and the uterus having been closed, the gall bladder was both visualized and palpated. There were no palpable stones. A general exploration of the abdomen was carried out at this time and the kidneys described

as "grossly normal in size and position; no induration about the duodenum; no enlargement of the spleen and liver edge smooth and firm." Following cesarean section, she recovered uneventfully and was discharged.

She was well for three weeks, but five days prior to the third admission the patient began having similar pain in the upper abdomen followed by increase in pain and persistent nausea and vomiting. Clinical diagnosis of acute cholecystitis was made and again she was placed on conservative management. Because her symptoms did not improve markedly, cholecystectomy was performed on the fifteenth of October. The operative note states: "On opening the abdominal cavity, approximately 1,500 c.c. of straw-colored fluid was obtained. The entire peritoneal cavity was studded with grayish 1 to 2 mm. tubercles. The gall bladder was thickened and no stones could be palpated. The common duct was extremely large, measuring approximately 1.5 to 2 cm. in diameter. Upon opening the common duct, numerous small, caviar-like stones were obtained. The pancreas was normal. Complete investigation of the lower abdominal cavity was not carried out since

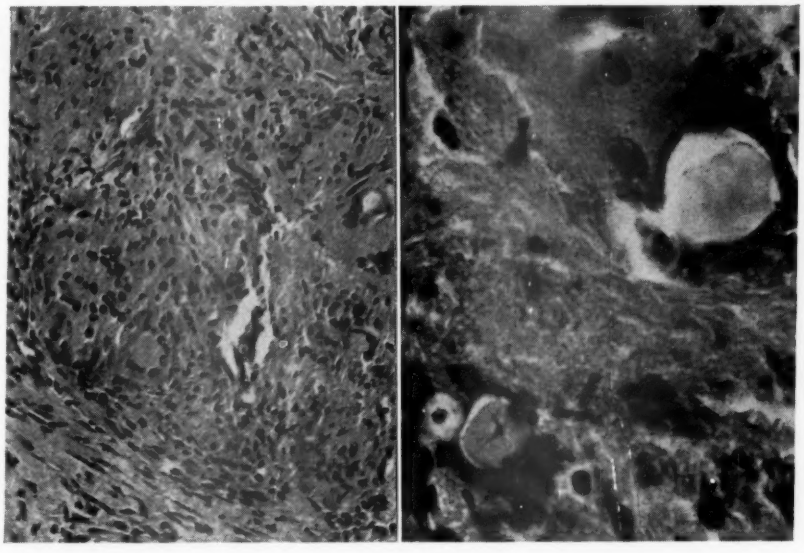

Fig. 3. Fig. 4.

Figs. 3 and 4.—Case 1. Peritoneal nodule. Granulomatous response to starch powder granules appearing within giant cells. Hematoxylin and eosin (×180 and ×770).

this patient had a cesarean section 4 weeks ago and it was felt not wise to do a complete lower abdominal examination at this time. Biopsy was obtained of the tubercles. After this, cholecystectomy and choledochostomy were carried out." The abdominal fluid was sterile after three days and was negative for acid-fast bacilli. The patient recovered uneventfully and was discharged on the twenty-eighth of October. In follow-up, she has remained asymptomatic.

The pathologic report on one of the biopsied nodules was: "Chronic cholecystitis with cholelithiasis. Portion of fibrous tissue (peritoneal surface of omentum) with granulomata and foreign bodies." The description of the microscopic histopathology includes the mention of a generalized fibrosis of the tissue with multiple granulomata, some of which were necrotizing. Foreign body giant cells, epithelioid cells, and lymphocytes contributed to the formation of the nodules. Situated throughout the specimen were small, round, faintly pink-staining bodies having the same appearance as the granules of absorbable starch glove powder (made up into a cell-block with serum). Both were anisotropic. The gall bladder did not show any of this material on the surface or any foreign body reaction (Figs. 3 and 4).

CASE 2.—B. D., a 37-year-old white woman, was admitted to Hartford Hospital on Jan. 9, 1955, for exploration of a mass in the right upper quadrant. She had first noted a swelling eight years previously. It had caused no symptoms, but it had grown in size over the past few years. Exploratory laparotomy and biopsy of the mass three months previously at another hospital on Oct. 22, 1954, revealed it to be a benign hepatoma of the liver, and she was referred to this hospital for definitive surgery. On Jan. 12, 1955, a partial resection of the right lobe of liver and cholecystectomy was performed. No adhesions were noted at the time of the operation. The 15 by 13 cm. mass of liver tissue removed was grossly normal, but microscopically, in addition to changes consistent with the diagnosis of benign hepatoma, there could be seen on the surface foreign body granulomata containing small round granules compatible with absorbable starch powder. The majority of the granules were found in the vicinity of suture material where there was scarring but no inflammatory reaction, except about the granules themselves (Figs. 5 and 6). The patient did extremely well postoperatively, considering the extensive surgery, and was discharged on February 6.

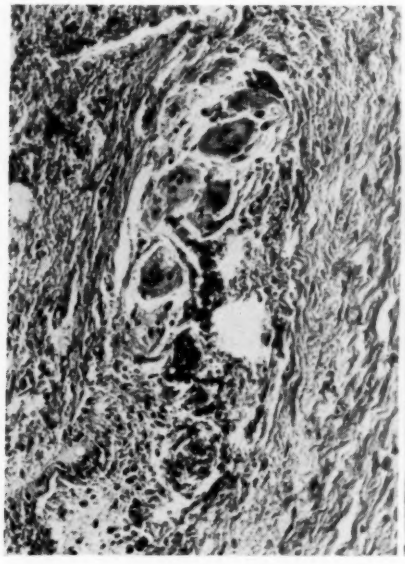

Fig. 5.

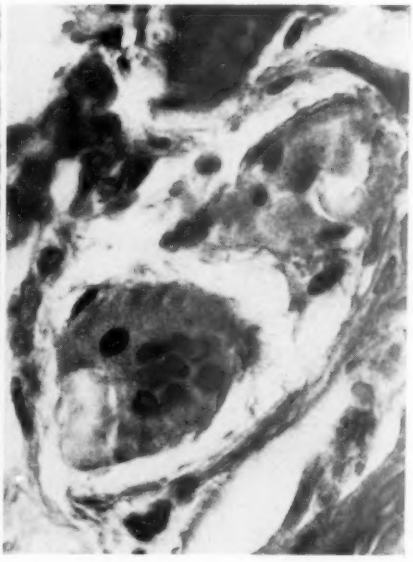

Fig. 6.

Figs. 5 and 6.—Case 2. Surface of liver. Granulomatous response to starch powder granules appearing within giant cells. (This reaction principally near silk suture material not shown.) Hematoxylin and eosin (×180 and ×770).

CASE 3.—G. H., a 61-year-old white woman, was admitted to the hospital on Dec. 26, 1954, with symptoms of two years' standing suggesting gall bladder disease. A cholecystogram had been performed in November which revealed the presence of a large calculus and a well-visualized gall bladder. On December 29, the patient had a cholecystectomy and a biopsy of the liver because it appeared somewhat irregular to the surgeon. This proved to be normal liver tissue and the gall bladder was chronically inflamed. At the time of operation, the surgeon did a general exploration, including the right lower quadrant, in an effort to do an appendectomy, but the cecum could not be mobilized. Otherwise, the area was unremarkable. The patient was discharged after an uneventful postoperative recovery, on Jan. 6, 1955.

Following discharge, she was well for ten days, then began to have anorexia, bloating, and low back and bilateral flank pain, and a feeling of "gas in the abdomen." This was accompanied by some fever. The patient was readmitted and was seen to be distended. A Levine tube relieved the distention. Small intestinal x-ray studies revealed the presence of a small bowel obstruction in the upper jejunum approximately 12 inches from the ligament of Treitz, and, subsequently, on the fourteenth of February, through a

right rectus incision, loops of small bowel were found adherent in the right lower quadrant and the omentum adherent to the lateral abdominal wall. Also, many 1 to 2 mm. sized nodules were seen on the serosal surfaces of the bowel and lateral peritoneal wall in this region. Dilated loops of bowel were seen proximal to these adhesions. These were released. The appendix was exposed and removed. The patient did well postoperatively and was discharged on February 15. Pathologic report of the appendix showed a foreign body reaction and granulomata on the surface of the appendix. This reaction was centered about small, round, foreign material compatible with absorbable starch powder granules (Figs. 7, 8, and 9).

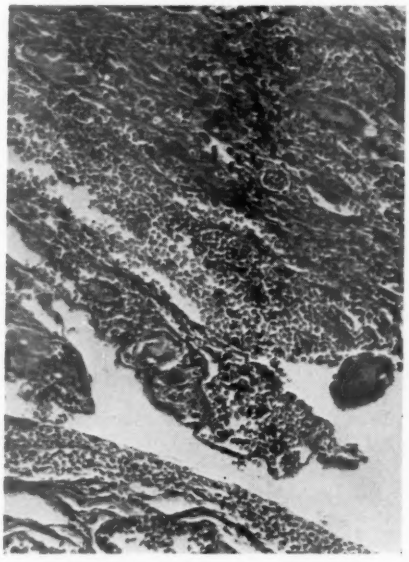

Fig. 7.

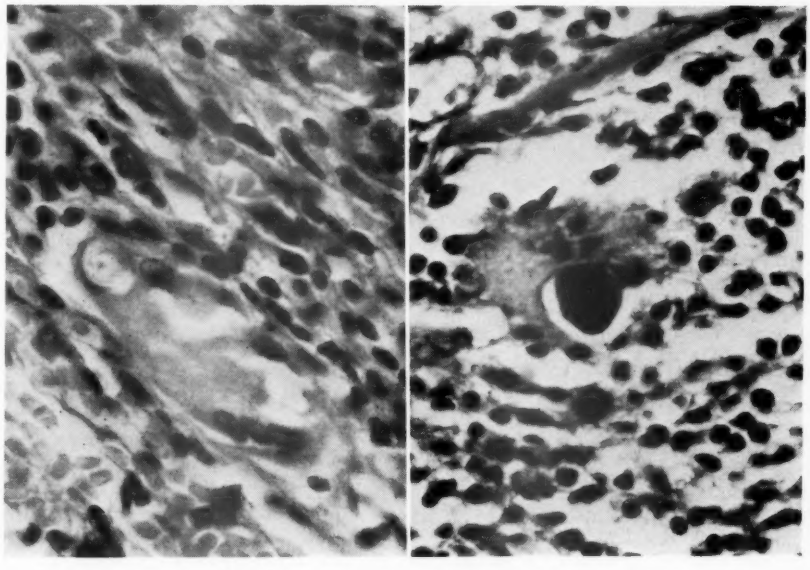

Fig. 8. Fig. 9.

Figs. 7, 8, and 9.—Case 3. Surface of appendix. Granulomatous response to starch powder granules appearing within giant cells. Hematoxylin and eosin (×180 and ×770) and PAS (×770).

DISCUSSION

Upon reading these case histories, the first question that immediately comes to mind is that of the manner of using the powder in the operating room.

Case 1.—The cesarean section was carried out in the operating room on the delivery floor. Here the custom is to open the packets of powder over a waste-basket in a corner of the operating room itself and there is obvious powder all over the floor in that region. With the presence of air-conditioning, with the exhaust outlet in the ceiling, the possibility of powder particles being carried over the operating area is a real one. (This practice is now being discontinued, the powder being opened in the scrubroom adjacent.) The gloves are always rinsed.

Case 2.—The biopsy of the liver was performed in another hospital in which it is the practice to open the powder packet in a corner of the operating room. The gloves are usually rinsed.

Case 3.—In the general operating rooms, in one of which this patient was operated upon, powder is applied in the scrubroom, so the important source of contamination would have to come from the glove surfaces. The gloves are often rinsed, but they were not rinsed in this specific case.

There would seem to be two points here. Is the powder envelope opened and used in the scrubroom or directly in the operating room, and, second, does the operating team rinse their gloves? None of these cases involved any grossly discernible contamination of the wound with the powder as far as any of the surgeons could determine, and yet there are these three proved instances of definite contamination followed by inflammatory response severe enough in two of the three cases to be the apparent cause of ascites or intestinal obstruction.

Case 2 raises an interesting question. Did the presence of the suture material on the liver surface (with the subsequent fibrosis) constitute a local irritant sufficient to delay absorption of the starch powder so that it was still present after seventy-nine days, it, in turn, acting as an exciting cause of foreign body response?

Now that the members of the Pathology Department in the Hartford Hospital are "sensitized" to this problem, not a day goes by that study of the microscopic slides of surgical specimens does not reveal the presence of starch powder granules. Usually, it is clear that the deposition of the powder occurred during the current operation, but there has been occasion in which many BIO-SORB granules have been seen against a chronic inflammatory or even granulomatous background, and it becomes necessary to differentiate between that powder present from a previous operation which is causing the inflammatory response and that powder making its appearance at the present operation. There are two criteria employed. First, the older granules are

usually less regular in shape and are less acidophilic, becoming rather faint-staining with eosin, whereas the fresh powder granules are quite pink-staining. Second, if the powder is to be incriminated as the exciting factor in the granuloma formation, it must be present within foreign body giant cells. Recently, during a hysterectomy, a portion of omentum adherent to the uterus was removed and revealed many starch powder granules against an inflammatory background. But the abundant numbers of granules were quite acidophilic, were not limited purely to those areas of chronic inflammation, and there was no foreign body response (Fig. 10). The patient, incidentally, had not had a previous operation.

The purpose of this paper is to bring to the forefront, in support of Lee and others, the fact that absorbable starch material is not the completely harmless glove lubricant popularly supposed, but that all possible precautions must be employed to obviate wound contamination, whether by direct glove contact or spread by air currents. It, of course, is obvious to all that the starch glove powder is greatly superior to talc, as witnessed by the rarity of known cases of complications caused by it in a relatively large general hospital, where it has been used in place of talc since 1948.

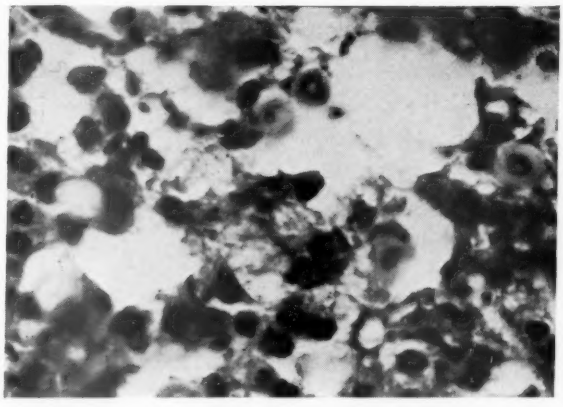

Fig. 10.—Omental tissue with chronic inflammatory reaction and many starch powder granules coincident with hysterectomy (see text). Hematoxylin and eosin (×770).

SUMMARY AND CONCLUSION

1. A brief history of the development of absorbable starch glove powder and its advantages is given.

2. The fact is stressed that until absorption takes place, the material is just as much of a foreign body as talc.

3. Three cases of granulomata due to absorbable starch powder are reported.

4. A brief discussion of ways of preventing or minimizing the frequency of such occurrences is given.

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THE INHIBITION OF HUMAN PANCREATIC SECRETION BY CARBONIC ANHYDRASE INHIBITOR

A Case Report

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THE role of carbonic anhydrase in the production of pancreatic bicarbonate has been suspected by physiologists and surgeons for many years. This concept has been based upon the rapid rate of production of bicarbonate by the pancreas, suggesting an enzymatic phenomenon. In addition, the pancreas has been found to be rich in carbonic anhydrase, an enzyme found widely distributed in the body. Evidence of a direct type awaited production of a potent and effective carbonic anhydrase inhibitor which did not have confusing side effects. Such a material, a modified sulfonamide derivative without bacteriostatic activity, was synthesized a few years ago and is now widely distributed under the name Diamox. When this product became available for investigative purposes, the effects of large but not toxic doses upon the pancreatic secretions of experimental animals were studied.[1] It was found in the experimental animal that Diamox is capable of markedly inhibiting water and bicarbonate secretion by the pancreas, although it did not apparently have any primary effect upon enzyme production. To our knowledge, however, there has been no report of a well-regulated trial of carbonic anhydrase inhibitor upon human pancreatic secretion. The present report is such a study.

CASE REPORT

The patient was a 23-year-old man who entered the hospital in December, 1953, with a long history of upper abdominal pain. The patient was admitted early in the course of an exacerbation of acute upper abdominal pain, and at the time of admission the serum amylase was significantly elevated. After controlling the acute bout of pancreatitis by nonoperative measures, a diagnosis of recurrent pancreatitis was established. There was patchy calcification in the region of the head of the pancreas disclosed by x-ray studies. There was marked enlargement of the head of the pancreas with flattening and widening of the duodenal C-loop and anterior displacement of the stomach and duodenum. There was, in addition, evidence of chronic cholecystitis with cholelithiasis, represented on cholecystogram by multiple small gall bladder calculi. After intensive preparation, the patient was taken to surgery where, after careful exploration, the following procedures were carried out: cholecystectomy with exploration of the common duct; transduodenal sphincterotomy; T-tube drainage of the common duct; and Pezzer catheter drainage of a large cyst in the head of the pancreas. The patient had a relatively uneventful and benign postoperative course. Drainage of pancreatic secretion from the cyst in the pancreatic head, however, was abundant and remained constant. Approximately ten days

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after operation, contrast medium was instilled into the pancreatic cyst by way of the draining catheter and it was demonstrated that a complete obstruction of the pancreatic duct existed between the cyst and the ampulla. The distal duct system emptied into the cyst. Drainage per catheter therefore represented either the total pancreatic secretion or a large and constant aliquot of it (Fig. 1). The drainage from the pancreas was carefully measured at frequent regular intervals over a period of four days. It was quite consistently sustained at 500 to 600 c.c. per twenty-four-hour period under the conditions of the study. Following this, the patient received Diamox in a dosage of 75 mg. per kilogram of body weight per twenty-four hours, given by mouth in divided doses. The medication was tolerated well and, during the entire course of seven days, the patient's only untoward complaints were moderate headache and some slight dizziness. The latter persisted only for the first two days during which he received the drug. No particular effect upon pancreatic secretion was observed during the first twenty-four hours. But subse-

Fig. 1.—Pancreatic cystogram demonstrating communication between catheter-drained cyst and distal duct system. No drainage into duodenum demonstrated.

quently there was a marked fall in the volume of pancreatic secretion per twenty-four-hour period. At the end of forty-eight hours, the volume of secretion had fallen to approximately 350 c.c. Within seventy-two hours it had fallen to approximately 220 c.c. and remained consistently between 200 and 300 c.c. each twenty-four hours over a four-day period. Amylase determinations made upon pancreatic drainage before and after the exhibition of Diamox did not disclose any change in the amylase concentration. At the end of the seven-day course of Diamox, further surgical procedure being contemplated, the cyst was reinjected with contrast material. This indicated that obstruction still existed proximal to the pancreatic cyst. The situation had in no way changed since the earlier study, and the drainage from the cyst still represented the same aliquot of total secretion. Following this, and with discontinuation of the Diamox therapy, pancreatic

secretion returned to original control volumes within forty-eight hours and transiently rose above the normal volume for the following forty-eight hours. It then returned to the normal pre-Diamox levels (Fig. 2).

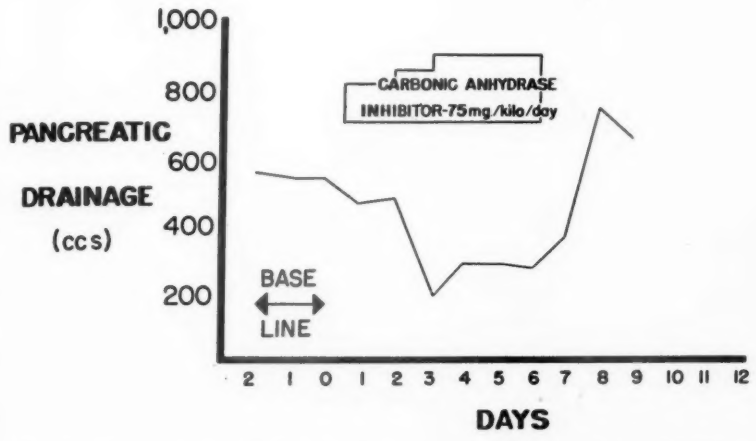

Fig. 2.—Graphic summary of influence of carbonic anhydrase inhibitor on the daily volume of drainage from a pancreatic fistula.

DISCUSSION

The effect of Diamox on the pancreatic secretion of a human subject with a surgically produced pancreatic fistula is reported. Observations were made on this patient in whom drainage of a pancreatic cyst represented either total pancreatic secretion or a constant aliquot thereof. Diamox in effective but not toxic doses was administered to this patient orally. A significant and marked fall in volume of secretion resulted within twenty-four hours after the initiation of Diamox administration. The diminution in secretion amounted to a reduction to approximately 35 per cent of control values. This fall in pancreatic secretion persisted during a five-day trial of the drug. Following discontinuation of the drug, measured volume of pancreatic secretion returned to normal control volumes. Repeated radiologic examinations indicated that there was no essential change in the area of the pancreas drained through the cyst. It would thus seem that carbonic anhydrase inhibitor has the same depressing effect upon human pancreatic secretion as has been reported in the dog. This of course leads to interesting speculation as to the possible usefulness of carbonic anhydrase inhibitor in the therapy of pancreatitis. Minimization of pancreatic secretion is an important objective in the treatment of pancreatitis.

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THROMBOANGIITIS OBLITERANS IN WOMEN

Report of Two Cases

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THROMBOANGIITIS obliterans (Buerger's disease) is an inflammatory disease, which may involve any artery or vein in the vascular tree. According to Boyd and associates,[1] it accounted for approximately 1.6 per cent of 472 cases of obliterative arteritis of the lower extremities. It is predominantly a disease affecting young men. In a recent review of the literature, Smith and co-workers[2] were able to collect 60 cases in women, but only 9 of these had been confirmed histologically. Undoubtedly, the disease exists in many women, but it is coaxed into the remissive stage without being diagnosed. A review of the records of vascular disease at the Ochsner Clinic since 1942 revealed only 2 cases of histologically proved thromboangiitis obliterans in women. Because of the rarity of this disease in women, these two cases will be described in some detail.

CASE REPORTS

Case 1.—Mrs. H. L., aged 29 years, came to the Ochsner Clinic April 13, 1942, complaining of cramping pain in her left foot and leg, precipitated by exercise and relieved by rest. Black and blue spots frequently developed spontaneously over the left ankle. Although she had been ill approximately two years, her activities had not been greatly restricted until six months previously. So acute had her condition become the week before examination, that minimum exercise produced excruciating pain. Although the condition affected the left foot predominantly, the right foot was also involved to a moderate degree. The patient had smoked one package of cigarettes daily for a number of years.

Examination on admission revealed definite cyanosis of the large and second toes of the left foot when placed in the dependent position. Mild rubor was evident over the remaining toes. Pulsations in the dorsalis pedis, posterior tibial, and popliteal arteries were diminished bilaterally, but more so on the left. A clinical diagnosis of thromboangiitis obliterans was made.

The patient was advised to follow a conservative regimen, consisting of two ounces of whiskey each day, heavy cotton or wool socks for protection and added warmth, a heating pad to the abdomen at night, and absolute discontinuance of smoking. When seen three months later, the patient reported that the cramping pains in the feet had been relieved.

When seen again Sept. 9, 1947, the patient complained of repeated infections about the toenails of both feet and the thumbnail of the right hand. She had recently injured the small toe of the left foot, and subsequent infection necessitated the removal of the toenail. Since this injury, agonizing pain in the left foot had made rest impossible.

Physical examination disclosed severe circulatory insufficiency of both feet with evidence of superficial gangrene in the distal phalanx of the fifth toe, surrounded by cellulitis which extended into the foot. Pulsations were absent in the dorsalis pedis and posterior

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A.

B.

Fig. 1.—Case 1. *A*, Photomicrograph showing thrombosis of left femoral artery and pronounced undulation of elastica intima (×40; reduced ¼). *B*, Photomicrograph showing round cell infiltration, undulating elastica intima, and perivascular fibrosis (×40; reduced ¼).

tibial arteries bilaterally, and in the left femoral and right radial arteries. Postural color changes with associated atrophic skin and nails were evident over both feet. Similar changes were present in the finger tips of the right hand.

On September 13, the second, third, and fourth lumbar ganglia were removed. Three days later, the fifth toe of the left foot was amputated. Because the gangrenous process persisted despite rigorous therapy, six days later the left leg was amputated above the knee and right lumbar ganglionectomy was performed. The microscopic diagnosis was thromboangiitis obliterans (Fig. 1, *A* and *B*). The patient was discharged from the hospital on October 31, after an uneventful postoperative course. Remission was still evident when the patient was last contacted seven years later.

CASE 2.—Mrs. J. C. F., aged 27 years, came to the Ochsner Clinic in December, 1953, complaining of pain in the left foot. Ten months previously, she had begun to experience cramping and extreme fatigue in the calves of the legs, which were precipitated by exercise and relieved by rest. A few months later, she noted tingling in the left large toe, followed shortly by "reddish blue" discoloration of all toes. She also experienced intermittent periods of swelling in the feet, which subsided spontaneously. The toes of the left foot became so tender that she was unable to endure pressure of sheets or blankets. Sensitivity to changes in the external temperature had not been noted. Her local physician made a presumptive diagnosis of Raynaud's disease. She was advised to take vascular exercises and discontinue smoking, and a vasodilating drug was prescribed. After a short time, during which she noticed little improvement, she discontinued the exercise and medication, and resumed smoking.

During the course of her illness, there appeared over the left thigh and leg small, red, tender areas which caused little difficulty and would subside spontaneously. Symptoms became increasingly more severe until the time of admission, when her left foot was so extensively involved and tender that walking was impossible. Narcotics were required for relief of pain. Elevation of the extremity to bed level increased the discomfort, whereas a dependent position resulted in slight relief. Recently, a small dusky area had appeared immediately below the left medial malleolus, and a similar area developed on the lateral aspect of this foot proximal to the fifth metatarsophalangeal joint. The patient had lost 30 pounds during the year before admission.

There was no family tendency toward peripheral vascular disease. The patient had had a mild fungous infection of both feet for a number of years. She had smoked approximately one package of cigarettes a day since the age of 13.

On physical examination the patient appeared acutely ill and much older than her 27 years. Physical abnormalities were limited to the lower extremities. The skin appeared scaly and felt cold to the touch. The toenails were thickened and deformed and fungous infection was evident between the toes. The toes of both feet were cyanotic and flushed in dependency, and cadaveric on elevation. The left foot was moderately edematous. A small area of gangrene, 1 cm. in diameter, was present just inferior to the left medial malleolus; a similar area was evident on the lateral surface of this foot at the base of the fifth toe (Fig. 2). There was global atrophy of the legs and thighs. The left foot was obviously the most severely involved. Palpation of the arterial pulsations in the lower extremities revealed diminished femorals with total absence of pulsations distally. Results of all laboratory examinations, including an electrocardiogram, were within normal limits.

The patient was admitted to Ochsner Foundation Hospital Dec. 8, 1953, and treated conservatively. The following day a polyethylene tube was inserted into the left lumbar region to maintain continuous paravertebral block, and 10 c.c. of a 1 per cent solution of Xylocaine was instilled through this tube at six-hour intervals. Within five to ten minutes following injection of the Xylocaine, complete relief of pain was obtained and lasted four to five hours. The rubor of the toes was slightly decreased and the foot was definitely warmer. However, the objective results were not proportional to the dramatic relief of the pain.

Since there was no evidence of stable improvement, on December 14, under spinal anesthesia, left lumbar sympathectomy (second, third, and fourth lumbar) was performed. On the first postoperative day, the left foot was no longer painful even when maintained at bed level. Soreness and tenderness replaced the previous numbness, and the extremity felt moderately warm. An area of impending gangrene had developed around the nail of the large toe on the left foot. The plantar surface of this toe appeared cadaveric. With the exception of the disappearance of edema, there had been far less objective improvement despite the pronounced symptomatic relief.

Fig. 2.—Case 2. Photograph of legs on first admission showing atrophic changes in the skin and nails with 1 cm. area of gangrene over left medial malleolus, edema of left foot, and global atrophy of legs.

By the fifth postoperative day, the area of impending gangrene around the left great toenail had become more definite, and the patient complained of intermittent burning and itching in this region, requiring a mild sedative for relief. She suffered a superficial "sheet burn" on the right lateral malleolus that showed no signs of healing. The color of the

right foot improved somewhat for the first twenty-four hours postoperatively, but then reverted to its original state. Symptomatic improvement was sufficient to justify discharge on December 20.

On the fourth day at home the patient again experienced intermittent episodes of burning and itching in the region of developing gangrene of the left big toe. The burning was described as being like a hot coal pressed to the big toe. These episodes became more frequent and were severe enough to cause her to faint on two occasions. She again required narcotics for relief. The right foot was asymptomatic except for occasional tingling in the right big toe.

On Jan. 5, 1954, the patient was readmitted to Ochsner Foundation Hospital. Examination revealed pronounced rubor of the left forefoot with dry gangrene of the distal half of the big toe (Fig. 3). At the patient's request a below-knee amputation was performed January 8. Examination of the vascular tree of the amputated extremity showed that the posterior tibial artery, nerve, and vein were bound together by scar tissue; the artery was completely occluded. The dorsalis pedis artery was extremely small and thickened. Microscopic diagnosis was Buerger's disease (Fig. 4).

Fig. 3.—Case 2. Photograph of patient's legs three weeks after left lumbar sympathectomy showing dry gangrene of left big toe, bilateral edema, and abrasion from sheet over right lateral malleolus present since first admission.

The patient's general condition improved remarkably after operation. She had no pain except for mild phantom itching in the region of the big toe of the amputated extremity. The stump healed well, and she was discharged January 24, to return at a later date for right lumbar sympathectomy. She had stopped smoking, and her weight on discharge was 82 pounds.

The patient convalesced satisfactorily at home. Her general condition improved; the sheet burn over the right lateral malleolus healed. However, the rubor over the right foot and toes remained the same. Her only complaint referable to the right lower extremity was intermittent tingling of the big toe and soreness over the plantar surface of the foot when she walked.

A.

B.

Fig. 4.—Case 2. *A*, Photomicrograph showing thrombosis of left posterior tibial artery with pronounced tortuosity of elastica interna (Verhoff's stain) (×40; reduced ¼). *B*, Photomicrograph of posterior tibial artery and vein. Verhoff's stain shows vascular thrombosis and perivascular fibrosis. Prominent vasa vasorum in tunica media of artery (×40; reduced ¼).

She was readmitted to Ochsner Foundation Hospital June 18, 1954, for evaluation and right lumbar sympathectomy. She had gained 32 pounds in weight and looked 27 years of age, rather than 45.

Physical examination revealed an increase in warmth of the right foot with no evident progression of the disease. Peripheral pulsations remained the same (none palpable below the femorals). Results of laboratory examinations, including electrocardiogram, were well within normal limits.

On June 21, right lumbar sympathectomy was performed. There was little change in color or warmth of the foot for the first twelve hours, but the rubor was gradually replaced by a light pink color. There has been gradual increase in warmth of this entire extremity. The patient has been fitted with an artificial limb and is now rehabilitated. Six months postoperatively further improvement is evident.

COMMENT

The signs, symptoms, and microscopic appearance of the disease in these two women justifiies the diagnosis of thromboangiitis obliterans. The etiological agent is not known, although both women had smoked excessively for many years. Since an increasing number of women have now been smoking for a period long enough for the disease to develop, it will be interesting to see whether the incidence will increase in women.

Vascular insufficiency was so severe in these cases that medical management was of no benefit and remission could not be induced. Lumbar sympathectomy resulted in remarkable subjective relief but little or no objective improvement. In the second case, ischemic neuritis developed four days after sympathectomy and became increasingly severe, until amputation was carried out at the request of the patient. Sympathectomy on the less affected side, concomitant with prophylactic measures, such as elimination of tobacco, resulted in excellent immediate improvement.

Remission is characteristic of this mysterious disease and in time it may "burn itself out." Prediction as to the ultimate outcome in these patients is impossible; yet it is our opinion that this represents generalized disease which may become manifest in other vessels later.

SUMMARY

Two cases of thromboangiitis obliterans in women are presented. The diagnosis was confirmed histologically in both cases. Sympathectomy not only permitted amputation at a lower level but also was of value in initiating and maintaining remission.

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CARCINOMA OF THE JEJUNUM OCCURRING IN A CASE OF REGIONAL ENTERITIS

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IN 1932, regional enteritis was classified as a disease entity distinct from other nonspecific granulomas of the small intestine and colon.[1] The present case report is of interest because it is believed to be the first case of a carcinoma arising in the small intestine at the site of a stenosing granulomatous enteritis. It is reported for purely scientific reasons and not because it is believed in any way to modify the present attitude toward the surgical management of this disease.

CASE REPORT

R. G., a 30-year-old white man, was admitted to the service of L. G. on Feb. 14, 1953, with a two weeks' history of increasing constipation, abdominal distention, nausea, and vomiting.

Since the age of 11, this patient had been subjected to frequent bouts of crampy abdominal pain associated with marked, but nonbloody, diarrhea, followed by periods of relative constipation. Such episodes would last for several months and be accompanied by severe weight loss. In 1941, at the age of 18, the patient was told that he had ulcerative colitis. He was treated with a bland, low residue diet, and sedatives, regaining much of his original weight.

In 1942, he was inducted into the army following which there was a recurrence of his previous symptoms. Gastrointestinal studies at that time were negative and the patient was placed on antibiotic therapy, but without effect. In 1943, he was given a medical discharge as a psychoneurotic.

From 1946 to 1949, he was relatively asymptomatic. In 1949, following an operation for a supposedly acute appendicitis, he had again a recrudescence of mucous diarrhea and constipation. Psychotherapy in the ensuing three years afforded only slight relief. In October, 1952, four months before admission, study of the colon by sigmoidoscopy and barium enema revealed no abnormalities. A gastrointestinal series, however, revealed rigidity of the segments of small bowel involving the jejunum with areas of dilatation in between. A diagnosis of granulomatous ileojejunitis was made. At the time of admission, the clinical picture was that of an acute intestinal obstruction.

Physical Examination.—On examination the temperature was 98.4° F., pulse was 84, respirations 20, and blood pressure 120/80. The patient was a thin, poorly nourished, chronically ill man with a distended, tense abdomen. Visible peristaltic waves traversed the abdomen from left to right. Hyperactive peristaltic rushes were heard on auscultation.

Roentgenographic Examination.—An obstructive series revealed extreme distention of the jejunum with multiple fluid levels. Gas was present in the ileum and colon in small quantities. The roentgenograph gave the impression of acute and chronic small bowel obstruction which was not, however, complete.

Laboratory Examination.—This revealed evidences of a hypokalemic and hypochloremic alkalosis. The patient was intubated with a Miller-Abbott tube and the appropriate intravenous therapy undertaken to correct the abnormal chemistry. Following this procedure, the acute obstruction was relieved and the blood chemistry figures returned to normal. The

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patient was put on a low residue, high caloric, high protein, high carbohydrate diet and permitted to regain a more physiologic nutritional state. Two weeks later he was operated upon.

Operation.—A right paramedian incision was made. Commencing about 18 inches distal to the fossa of Treitz, a series of stenosing lesions with extreme dilatation of the intervening bowel was encountered. The distal segment of diseased bowel was located about 6 feet distal to the primary one. Distal to that point there was no evidence of diseased bowel. The entire segment of diseased bowel, both stenosing and dilated, was resected. There were numerous glands in the mesentery, but these felt soft and inflammatory. A side-to-side anastomosis was performed because of the extreme disparity in the diameter of the proximal and distal segments, the proximal segment appearing at least four times the width of the distal. There was no suspicion at the time that the lesion was anything but an

Fig. 1.—Operative specimen showing the typical changes of regional enteritis. In addition, the "sausage link" appearance of partial loop obstruction is seen.

inflammatory granulomatous jejunitis. The colon showed no abnormalities. The liver was not particularly explored but that portion which appeared in the wound showed no evidence of abnormality.

The patient made an uneventful recovery following operation.

Pathological Examination.—Gross: The specimen consisted of 150 cm. of jejunum composed of alternate loops of dilated and constricted bowel. There were three distinct areas of constriction measuring 2, 7, and 35 cm. in length. The bowel in these regions was thickened, rigid, and hoselike. The first area was 9 cm. from the proximal resected end. The second was 8 cm. beyond the first, and the third was 12 cm. beyond the second. The smallest constriction was sharply demarcated. The mesenteric fat over the constricted area was thick, boggy, and hyperemic, and it covered the antimesenteric border of the bowel over those regions that were involved by the inflammatory process. This change in the mesenteric fat was absent over the uninvolved areas. The lymph nodes in the mesentery were not enlarged (Fig. 1).

In the constricted area, the bowel wall was firm and measured up to 0.4 cm. in thickness. On section, the thickening was most marked within the submucosal region. The

Fig. 2.—Close-up of one of the constricted segments revealing the characteristic pebbling of the mucosa.

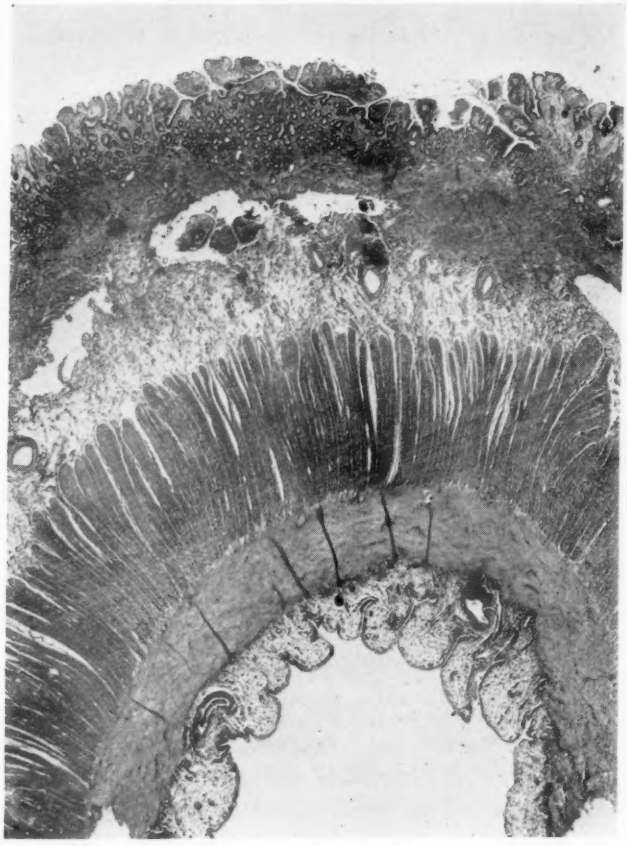

Fig. 3.—Low-magnification view through constricted segment. Submucosal edema, lymphocytic infiltration and fibrosis are apparent (×5).

lumen was greatly narrowed. The mucosa in these regions had lost its normal markings, and a finely pebbled nodular mucosal surface replaced the normal transverse folds. Small areas of superficial ulceration were present (Fig. 2). As the lumen increased in size toward the poles of the constricted segments, the wall gradually became thinner and the mucosa regained the transverse folds. There were three dilated loops of bowel measuring up to 20 cm. in length. Forty centimeters from the proximal resected end, and arising from the mucosa of the distal pole of one of the dilated loops, there was a firm, indurated tumor mass measuring 2 cm. in diameter.

Microscopic.—The hyperemic serosa was infiltrated with inflammatory cells, predominantly lymphocytes. The characteristic change in the wall was that of submucosal thickening as a result of edema, fibrosis, and lymphocytic infiltration (Fig. 3). No caseation, giant cell, or necrosis were noted. The muscle and mucosal layers were likewise thickened and contained foci of fibrosis which are not as marked as in the submucosa. The normal mucosal architecture was completely destroyed in the constricted areas where it was congested

Fig. 4.—Arrow points to nodule which, on section, revealed adenocarcinoma.

and infiltrated with aggregates of lymphocytes and mononuclear cells. This tumor mass, located 40 cm. from the proximal resected end, consisted of an adenocarcinoma arising from the mucosa and invading the bowel wall (Figs. 4 and 5). Cords of anaplastic tumor cells extend to and invade the serosa.

Second Admission.—The patient was readmitted in September, 1953, approximately six months following the initial procedure, complaining of pain in the epigastrium of about two weeks' duration. He had been in good health from the time of the operation until the appearance of the present symptoms. His temperature was 101° F. and had reached that level daily for the past two weeks.

Examination revealed the presence of a slightly tender, moderately firm mass in the epigastrium which moved with respiration. The mass measured about 10 cm. in diameter.

Operation.—An exploratory laparotomy was performed through a vertical paramedian incision. The mass was found to be a carcinoma involving the left lobe of the liver. Other metastatic nodules were present throughout both lobes. There was no evidence of tumor in the mesentery or at the site of the anastomosis. A wedge-shaped biopsy was taken from one of the hepatic nodules which on histologic examination showed adenocarcinoma. The histology resembled that of the carcinoma of the jejunum previously removed.

SUMMARY

A case of carcinoma of the jejunum with subsequent early hepatic metastases arising in a segment of bowel, the seat of a granulomatous jejunitis, is reported. The rarity of this complication in inflammatory granulomatous disease of the small intestine is stressed. This is in contradistinction to the relative frequency of carcinoma developing in cases of chronic ulcerative colitis. This difference is probably due to the fact that carcinoma occurs frequently in the colon and only very rarely in the small intestine.

Fig. 5.—Low-magnification view revealing adenocarcinoma arising in mucosa and invading bowel wall, immediately adjacent to an area of jejunitis (×11).

From a practical standpoint in the general treatment of regional enteritis, the indications for surgical intervention are not affected. Certainly, prophylactic surgery for the prevention of the eventual development of carcinoma does not appear to be warranted. Where multiple lesions exist, such surgery is, of course, impractical. In localized distal ileal lesions, the question of the advisability of resection vis-à-vis ileocolostomy with exclusion may be raised. Our attitude would be not to consider the remote possibility of such a complication as the determining factor. It should be stressed that no case of carcinoma arising at the site of regional enteritis has as yet been reported.

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Editorial

Bogey In Surgery

All surgeons have two hobbies, surgery and golf. They know what bogey means. A famous London surgeon, when about to perform his "specialité de la maison" which was the removal of a normal appendix through a one-inch incision, was wont to remark to his students, "Bogey for this operation is six minutes." That was twenty years ago. He is dead and so is his type of surgery. A surgeon's skill is now judged, not by the speed of his prestidigitation, but by the gentleness of his hands. His true worth is better assessed by a stroll through his wards the day after operation than by a visit to the operating room while he is at work.

If "operating by the clock" has become a bad joke, what is "bogey" in surgery now? Charles Mayo is said to have stated that "the most important result of a successful operation is a live patient." That was a momentous enunciation of a truth so obvious that few surgeons at the time had really paused to consider it. It would not strike with the same force today when corporeal survival can be assumed without question, when the causes of death in Mayo's day—shock, hemorrhage, sepsis, and postoperative pulmonary complications—have been abolished. Today we might restate his aphorism a little differently by saying that "the most important result of a successful operation is live tissues," that is, tissues that have been handled so gently that where they have been cut they present clean healthy surfaces, where they have been retracted they are unbruised, where they have been brought together they will unite with little scar tissue intervening. Bogey today is the avoidance of tissue trauma; it should be, but is it? One form of trauma that we tend to forget is the lapse of time. We have abolished operating by the clock; let us not put in its place operating by the calendar.

But surgeons cannot always achieve perfection. Sometimes the best result they can give is only the best possible in the circumstances. In the surgery of cancer, the most important result of an operation is not necessarily a live patient. The films have made us familiar with the concept of "a fate worse than death." Such a fate may well be the lot of a cancer patient who has been the victim of a successful operation that, by prolonging his life, has prolonged his suffering and exposed him to an agony which he would have been spared had the disease been allowed to proceed unchecked. Bogey in cancer surgery is not always a life saved or even a life prolonged; it is a life made more tolerable while it lasts and an ending made more serene when it comes.

—Sir Heneage Ogilvie

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

POSTBULBAR DUODENAL OBSTRUCTION IN ADULTS

ETIOLOGY, DIAGNOSIS, AND TREATMENT

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OBSTRUCTION of the duodenal bulb is frequently seen. Over 90 per cent of the cases are secondary to chronic peptic ulcer formation with stenosis. Roentgenologic evidence of obstruction in other portions of the duodenum immediately arouses uncertainty regarding etiology. Isolated cases of obstructing lesions involving the second, third, and fourth parts of the duodenum are seen, but the number and variety are too few for adequate experience in preoperative evaluation, and when confronted at surgery with such a lesion the mode of attack may be ill chosen.

It is the purpose of this article to give a comprehensive picture of various lesions causing duodenal obstruction so that a more rational approach to handling such patients may be had.

Obstruction of the duodenum may develop quickly or slowly. Symptoms and prognosis vary greatly with the speed of occlusion. Etiology differs for different ages. In infants and children developmental abnormalities, such as duodenal stenosis and atresia or duodenal bands associated with malrotation of the colon, are usually responsible, while neoplasm and inflammatory lesions are the most frequent causative agents in adults. Most congenital abnormalities with a definitive or latent ability for obstruction become evident long before adulthood. In adults the obstruction tends to be chronic and frequently one is acquainted with the condition when an acute high-grade obstruction develops in a patient with a chronic stenosing lesion. In general, the immediate prognosis is far better in chronic obstructions but eventual survival depends largely upon the patient's over-all condition and the degree of deadliness of the etiological process.

Adults with chronic obstruction tolerate great distention of the duodenum and stomach if the occlusion increases slowly. Pain, vomiting, and emaciation dominate the symptomatology. Pain varies from none to extreme and a markedly dilated stomach and duodenum are frequently associated with a minimal history of distress. Vomiting varies from none to repeated copious emesis.

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In slowly stenosing lesions one often elicits a past history of infrequent vomiting at irregular intervals with a marked increase in frequency and severity shortly before admission. If the obstructing process is chronic and high grade, the most constant symptom is emaciation, which is often extreme.

In reviewing the literature, isolated reports on many pathologic processes causing postbulbar duodenal obstruction are recorded. Table I lists conditions found to be responsible for obstruction. Such a listing, although helpful in a comprehensive evaluation of possible etiology, fails to point out which conditions are more apt to be responsible.

TABLE I. ETIOLOGY OF POSTBULBAR DUODENAL OBSTRUCTION IN ADULTS

A. Congenital Abnormalities
1. Congenital stenosis and diaphragm
2. Annular pancreas
3. Enterogenous cyst of the duodenum
4. Arteriomesenteric duodenal compression
5. Abnormal fixation at the ligament of Treitz
6. Congenital bands and ligaments
B. Inflammatory Abnormalities
1. Postbulbar peptic ulceration
2. Regional enteritis
3. Pancreatic cyst
C. Neoplastic Abnormalities
1. Carcinoma of the pancreas
2. Carcinoma of the ampulla of Vater
3. Carcinoma of the duodenum
4. Benign tumors of the duodenum
5. Sarcoma of the duodenum
6. Primary retroperitoneal tumor
D. Periduodenal Lymphadenopathy
E. Intermural Hematoma
F. Gallstone Obstruction of the Duodenum
G. Duodenal Diverticulum

CONGENITAL STENOSIS AND DIAPHRAGM

Development of the duodenum may proceed abnormally producing varying degrees of clinical duodenal occlusion, described as atresia, stenosis, and valve formation. Atresia, meaning complete absence of lumen, is not observed initially in adults. Stenosis and valve formation, depending upon the severity of occlusion, may be seen at any age. Stenosis in infants, although uncommon in the intestinal tract compared to atresia, has been found by Gross[24] to be most frequently observed in the duodenum. Usually any significant degree of stenosis becomes evident before adult life. Davies, Glass, and Roth[12] reported only 10 adult patients recorded in the literature who survived surgery. Most of these had symptoms of intermittent obstruction earlier in life. A duodenojejunostomy is the procedure of choice over gastrojejunostomy since, in the latter, the portion of duodenum above the obstruction may not be fully decompressed. In addition, alkaline duodenal juices are forced to traverse the normally acid stomach on the way to the jejunum. Although accomplished successfully,[12] a longitudinal incision through the strictural portion with a transverse closure is not recommended since suturing is carried out on abnormal tissue in the atretic area. Congenital valves or diaphragms are exceedingly rare and no references to such conditions in adult life could be found.

ANNULAR PANCREAS

Considerable interest is shown in annular pancreas, as it is the most common of the congenital abnormalities causing duodenal obstruction in adults. Wilson and Bushart,[62] in a recent review, reported a total of 31 surgical cases, of which 19 were adults. Many additional cases were found at autopsy in asymptomatic individuals. Men predominated two to one. Annual pancreas is rare in comparison with carcinoma arising in this region.

Aberrant pancreatic tissue is derived from faulty fusion of the ventral and dorsal analogue of the primitive pancreas and anatomically consists of a thin band of pancreatic tissue arising from the head and completely encircling the duodenum. Symptoms reflect the degree of obstruction. Many patients are free of symptoms throughout life, while others become symptomatic at varying ages. Frequently, indigestion, eructations, and vague epigastric pain are noted prior to the onset of frank duodenal obstruction. When symptoms first develop in adult life the obstruction is often related to peptic ulceration in the stenotic area of the duodenum.

The diagnosis is strongly suspected when roentgenologic examination with barium reveals a smooth, sharp, ringlike constriction in the region of the duodenal papilla with dilatation of the duodenum above and decreased caliber of the lumen below.

At surgery, the right side of the transverse mesocolon and the peritoneum covering the second portion of the duodenum are retracted to expose the involved duodenum. The surgical procedure of choice is a by-passing operation, such as a duodenojejunostomy. This adequately relieves the obstruction and carries less risk than direct attack on the constricting band. The experiences of most authors[45, 51, 62] with the excision of part or all of the constricting ring have been less satisfactory, and several instances of pancreatitis, pancreatic fistulas, and failure to relieve the obstruction have been observed.

ENTEROGENOUS CYSTS OF THE DUODENUM

Enterogenous cysts of the duodenum are almost unknown. Polson and Isaac,[46] in 1953, found only 21 cases in the literature and most were in infants and young children. Gardner and Hart[20] and Polson and Isaac,[46] however, have reported single instances of adults with duodenal obstruction due to this cause. In both instances, a long history of anorexia, vague upper abdominal distress, and vomiting were noted dating back to childhood.

Roentgenologic studies with barium demonstrated minimal dilatation of the stomach but an enlarged upper duodenum with a filling defect protruding into the lumen below this level. The surgical procedure of choice is removal of a large segment of the septal wall between the two lumens.

ARTERIOMESENTERIC DUODENAL COMPRESSION

Bockus[4] stated that arteriomesenteric occlusion is the most frequent cause of stasis in the third portion of the duodenum. Adults from 30 to 40 years of age of the asthenic, visceroptotic, lordotic body habitus are most frequently affected. Women predominate three to one. A mild degree of obstruction is

the usual finding. Anatomically, the condition occurs in human beings due to the caudal direction of the superior mesenteric vessels. The duodenum in this position crosses over both the vertebral column and abdominal aorta. If the root of the small intestinal mesentery is anatomically narrow, the tug of the mesentery may be sufficient to cause a bandlike constriction of the duodenum where it passes beneath the mesenteric pedicle. This is especially prone to occur in patients with marked visceroptosis and an exaggerated lumbar lordosis. Clinically, a prolonged history of attacks of indigestion with intermittent, incomplete high intestinal obstruction, alternating with periods of fairly good health, are almost invariably obtained. The symptoms are postprandial bloating, flatulence, and a sense of fullness. Nausea and vomiting are common. Pain may be either aching or colicky and usually is relieved by the knee-chest position.

The diagnosis is suggested by barium studies with fluoroscopy showing a churning movement of the fluid in the transverse duodenum with dilatation of the bowel and proximal retention of barium for several hours. An extensive trial of medical therapy consisting of complete bed rest, elevation of the foot of the bed, and knee-chest position after meals is advocated.[29] The goal is to increase the disposition of fat in the body and in the mesentery especially. However, if symptoms persist surgical relief is desirable. At surgery, on elevation of the transverse colon, a bulge of the third portion of the duodenum is present to the right of the small intestinal mesenteric pedicle. A duodenojejunostomy is the procedure of choice.

ABNORMAL FIXATION AT THE LIGAMENT OF TREITZ

Three cases of duodenal obstruction due to accentuation of the normal angle of the duodenojejunal junction associated with high or abnormal fixation of the ligament of Treitz have been described by Rosenblatt.[54] Nordentoft[43] described a similar case in a young child. This is apparently an exceedingly rare site for clinical obstruction, for no other reports were found in the recent literature. It is ascribed to ptosis of the abdominal organs including the third portion of the duodenum, with an increase in the acuteness of the duodenojejunal angle. Symptoms are similar to those to arteriomesenteric duodenal compression, and barium studies demonstrate an obstruction at the ligament of Treitz with dilatation of the duodenum proximally. Rosenblatt[54] reported complete relief of symptoms in 2 of 3 patients with division of the ligament of Treitz.

CONGENITAL BANDS LIGAMENTS

Comparatively frequent causes of duodenal obstruction in infants and young children are congenital bands associated with malrotation of the colon or congenital kinking of the duodenum with abnormal fixation. Very few of these individuals survive without surgical intervention, and congenital bands as a cause of adult duodenal obstruction are quite rare. Gregory, Priest, and Barron[23] reported a 22-year-old man with obstruction at the junction of the first and second parts of the duodenum due to a congenital band running from the neck of the gall bladder across the duodenum to the transverse colon. An

extreme degree of obstruction was present despite complete lack of symptoms prior to one month before surgery. I[50] have reported a 39-year-old man with marked kinking of the second portion of the duodenum with abnormal fixation due to congenital bands in whom symptoms of obstruction first occurred five months prior to surgery. The surgical procedure is usually confined to severing the adhering ligaments or bands which compress the lumen or maintain the bowel in a kinked position.

POSTBULBAR PEPTIC ULCERATION

Peptic ulceration of the distal duodenum is a relatively uncommon lesion which occurs most frequently in patients with histories suggesting ulceration but without lesions in the stomach or duodenal bulb. Portis and Jaffe[47] in 457 consecutive autopsies showing peptic ulcerations found only 5 per cent of the duodenal lesions beyond 5 cm. from the pylorus. Finklestein,[18] in reviewing the literature in 1950, found only 80 patients with postbulbar ulceration discovered by radiographic examination. This undoubtedly is due to failure in reporting this variant of the peptic ulcer process. Alvarez and Farinas[1] noted that men, as with bulbar ulcers, were more commonly afflicted, but observed that the average age of patients with postbulbar ulcers was 48 years, as compared with 33 years in the bulbar variety.

The most frequent site of ulceration is the medial aspect of the superior duodenal angle slightly within the initial portion of the descending duodenum. Frequency decreases on approaching the ampulla of Vater and becomes exceedingly rare beyond this point. A prominent pathologic feature is the rather deep penetration into the adjacent pancreas with its surrounding induration which together produce a relatively large inflammatory mass. A characteristic laboratory finding is an extremely high gastric acidity.[1]

Seventy-five per cent of the patients have a typical ulcer type pain which, although relieved greatly by food and alkali, is not as consistent and is more delayed than in uncomplicated bulbar ulcers.[1] Episodes of pain are more irregular and frequently a striking absence of characteristic pain in patients with advanced ulceration is noted. Postbulbar ulcerations have an outstanding tendency to hemorrhage profusely and easily even though pain is relatively minor.[5, 58] Alvarez and Farinas[1] observed hemorrhage to be three times as frequent in postbulbar (37 per cent) as compared with bulbar (12 per cent) ulcers. Lonergan and Kahn[53] reported massive hemorrhage in 7 of 10 patients. Duodenal stenosis and symptoms of pyloric obstruction are very common. Crymble[11] reported 4 cases of postbulbar ulceration with 3 instances of marked duodenal stenosis. Lonergan and Kahn[33] noted, on roentgenologic examination in all of their 10 cases, a definite narrowing and constriction of the lumen due either to muscle spasm or to scarring with constriction. Marshak and Dreiling,[40] although noting the tendency for obstruction, felt that complete obstruction due to this cause was very uncommon. Biliary and pancreatic obstructions have been found to be rare.[1]

On roentgenologic examination the most characteristic sign in a niche defect as in bulbar ulcers. Frequent contractions of the duodenum are seen at the

site of the niche and the contour of the wall is irregular. More frequent but less decisive in making a diagnosis is narrowing and constriction of the lumen with distortion of the mucosal pattern at the level of the ulcer. It frequently appears as a filling defect. Many patients have gastric dilatation or atony associated with the stenosis. Healing may give rise to persistent narrowing of the lumen which remains for a long period of time.

Management of postbulbar ulcers is similar to the bulbar variety. A strict medical regimen of diet, antiacids, antispasmotics, and anticholinergic medications is prescribed and, in most instances of uncomplicated ulcer, is successful.[1,33] In patients with massive hemorrhage or residual stenosis, subtotal gastric resection or vagotomy with gastrojejunostomy is the procedure of choice. If gastric resection is performed, removal of the ulcer from the pancreas should not be attempted due to added risk of pancreatitis or damage to the ampulla of Vater.

REGIONAL ENTERITIS

Chronic cicatrizing duodenitis is an extremely rare entity in contrast to its counterpart in the rest of the small and large intestine. Brown and Sims,[7] in 1954, were able to accumulate only 15 cases from the world literature. Gregg and Weisser[22] reported the average age of patients with duodenal involvement to be 28 years and noted that the usual symptoms of epigastric discomfort, gaseous eructations, upper abdominal crampy pain, nausea, and vomiting might easily be confused with those of peptic ulcer. Comfort and associates[10] observed four outstanding clinical features: (1) continuous or intermittent upper abdominal distress intensified by food intake and characterized by loss of weight, weakness, nausea, and vomiting; (2) diarrhea, steatorrheal in type; (3) gastric retention; and (4) signs of decreased absorption. A high percentage of all patients first presented themselves for diagnosis with symptoms of gastric and duodenal obstruction.

The roentgenologic picture shows a disturbed motility of a portion of the duodenum with an irregular, narrowed lumen with projections along its contour due to small multiple ulcerations. Not infrequently, skip areas with distal involvement are noted further down in the gastrointestinal tract. Too few cases have been seen to define adequately a surgical procedure of choice. Successful results have been reported with side-tracking procedures, such as gastrojejunostomy.[7]

PANCREATIC CYST

Extrinsic obstruction of the duodenum by a pancreatic cyst is exceedingly rare. Radiographic examination, although frequently demonstrating widening of the duodenal loop with displacement of the stomach forward and the transverse colon inferiorly, rarely demonstrates significant narrowing of the duodenum to create a more proximal dilatation. Loggan and Kleinsasser,[32] in a review of pancreatic surgery, reported 500 cases of pancreatic cysts recorded up to 1940. Histologically, several different types of cysts and pseudocysts may be found. Of these, about one-third are relatively asymptomatic and are discovered chiefly by the presence of a mass.[8] Pseudocysts, which constitute the

major group, are usually secondary to repeated episodes of acute pancreatitis associated with severe symptoms of upper abdominal pain, fever, nausea, vomiting, and anorexia. Large pseudocytes have been known to obstruct the pyloric outlet but cases with clinical symptoms of duodenal obstruction are almost unknown. Cattell,[8] in reporting experiences with 25 cases requiring surgical intervention, had not had a single patient with evidence of marked obstruction. Only 2 recent reports of duodenal obstruction due to pancreatic pseudocysts were found. McGrigor[35] reported 1 instance of obstruction at the junction of the first and second portions in a patient with chronic recurrent pancreatitis. A large cyst with a fibrous band extending from it across the duodenum was discovered. McMillan and Mason[36] reported a hemorrhagic pseudocyst obstructing the lower part of the duodenum. Barium studies demonstrated a highly dilatated stomach with a faint outline of the duodenal loop. The procedure of choice in cases of gastrointestinal obstruction is decompression of the cyst by marsupialization or internal drainage and severing any obstructing bands encroaching on the duodenal lumen.

CARCINOMA OF THE PANCREAS

Symptoms of duodenal obstruction as a first suggestion of pancreatic carcinoma are uncommon. Invading carcinoma sometimes causes a varying degree of compression of the antrum or duodenal bulb, but as a rule fails to result in prominent symptomatology. Beeler and Kirklin[3] reported that pancreatic carcinoma comprises 1 to 2 per cent of all cancers. This condition overwhelmingly strikes people over 50.[42] The head of the pancreas is involved in over 70 per cent of the cases.[6] Seventy of 167 patients reported from the Mayo Clinic demonstrated radiographic abnormalities in the doudenum, with 14 showing actual obstruction.[3] By far the most frequent site of duodenal involvement was the cap, with the second portion demonstrating narrowing in only 2 instances. Severe degrees of obstruction are occasionally seen, for Marshak and Dreiling[40] reported 4 patients, all women, entirely asymptomatic until the offending lesion produced profound obstruction of the upper gastrointestinal tract.

Neoplasms of the pancreas may produce obstruction anatomically either by exerting external pressure, thus narrowing the lumen, or by invading the submucosa and mucosa directly. To evaluate this condition, both clinical and roentgenologic findings must be reviewed. Usually, in carcinoma of the head of the pancreas, constant boring pain is present in the epigastrium or right upper quadrant, perhaps with radiation to the back. Since the carcinoma arises primarily from the head of the pancreas and must become fairly extensive prior to involving the duodenum, an advanced stage in the disease process is usually present with jaundice, pain, weight loss, and a palpable mass previous to the onset of clinical symptoms of obstruction.

Roentgenologically, duodenal deformity is the most frequent finding in the experience of Beeler and Kirklin,[3] with the defect usually on the concave aspect of the first and second parts of the duodenal loop with irregularity

localized to a small segment of intestine. When obstruction develops, the nature of the underlying lesion becomes difficult to determine, for obstruction produces proximal dilatation of the duodenum and stomach with marked degrees of occlusion. With less severe degrees of narrowing, the mucosal pattern of the duodenum may show an external pressure defect with flattening out of the lumen in contrast with the typical intrinsic type of mucosal alteration seen with carcinomas of the ampulla of Vater and duodenum.

Since obstruction of the duodenum secondary to carcinoma of the pancreas is usually associated with an advanced malignancy, the best available treatment is a palliative gastrojejunostomy and cholecystojejunostomy to relieve duodenal and biliary obstruction.

CARCINOMA OF THE AMPULLA OF VATER

Clinical obstruction of the duodenum due to carcinoma of the ampulla of Vater is practically unknown, for both the gross characteristics of the tumor and its immediate location to the biliary tract are inconsistent with a chronic stenosing lesion. Whereas pancreatic malignancies tend to invade and infiltrate tissues, the typical carcinoma of the ampulla of Vater is fungating or polypoid. The characteristic roentgenologic picture is a filling defect in the region of the ampulla with no appreciable narrowing of the lumen. Because of the proximity of the biliary tract, clinical jaundice appears early and surgical exploration or death ensues long before clinical symptoms become manifest. Review of the recent literature failed to disclosed a case of significant duodenal obstruction in a previously unattended lesion of the ampulla of Vater.

CARCINOMA OF THE DUODENUM

Carcinoma of the duodenum represents only 0.25 per cent of all carcinoma[55] or about 3 per cent of intestinal cancers.[16] Eger[17] estimated that carcinoma of the stomach was 100 times more common. Hoffman and Pack[28] found in a series of 228 cases of carcinoma of the small intestine that 45 per cent of the lesions were in the duodenum. As in carcinomas of other locations, most patients were in late middle to advanced years. Anatomically, the descending portion of the duodenum is most frequently involved. Pathologically, three types of carcinomas are seen: (1) a scirrhous, annular tumor with overproduction of fibrous tissue tending to constrict and obstruct; (2) a bulky polypoid intraluminal mass prone to ulcerate with partial obstruction and hemorrhage; and (3) a colloid carcinoma with mucoid degeneration.

Symptomatology depends upon gross characteristics and location in the duodenum. Scirrhous, annular carcinomas are most frequent and are characterized by duodenal obstruction with infrequent and late metastases, while the bulky polypoid tumors are usually associated with upper gastrointestinal hemorrhage and symptoms suggestive of peptic ulcer. Kleinerman, Yardumian, and Tamaki[30] noted distinguishing anatomic and clinic characteristics among lesions of the suprapapillary, peripapillary, and infrapapillary regions. Carcinomas of the suprapapillary portion commonly have an abrupt onset of

symptoms, whereas neighboring cancers of the antrum customarily develop symptoms more gradually. The peripapillary lesions tend to encircle the bowel before clinical jaundice becomes evident, in contrast with carcinoma of the ampulla which causes early biliary tract obstruction. Tumors of the infrapapillary area usually are of the annular constricting variety and marked gastric dilatation with episodes of acute pain and severe vomiting are part of the clinical picture.

In general, symptoms are varied and nonspecific. The majority of patients have vague epigastric distress, anorexia, weight loss, slight pain, and weakness, while nausea and vomiting are not uncommon. Jaundice is a late sign and occurs after the mass has become quite large. Since 90 per cent of the tumors originate from the mucosa, pressure is produced from within the lumen. The duodenal loop on roentgenologic examination does not change, but the mucosal pattern is drastically altered. The duodenal lumen may be widened locally by the growing polypoid tumor or constricted with proximal dilatation by the constricting variety.

A more optimistic prognosis with radical surgery can be had with obstructing duodenal carcinoma than with cancer of the pancreas. Exploration with the possibility of radical pancreatoduodenectomy should be undertaken in all patients, for it is well known that the scirrhous constricting type metastasizes infrequently and late. If obstruction is severe and of long duration, temporary gastrojejunostomy may be of value in preparation for extensive cancer surgery.

BENIGN TUMORS OF THE DUODENUM

Benign duodenal tumors are very rare. Hoffman and Grayzel[27] collected only 66 cases from the literature in 1945. The two most common were adenomas and myomas with 21 to 11, respectively. Eleven histologically different, benign neoplasms comprised the remainder. Symptoms were usually those of melena, ulcer type distress, or were asymptomatic.[57] Rarely did the neoplasm grow large enough to create primary obstruction[2, 37] or to be responsible for obstruction secondary to intussusception.[31, 61] The surgical procedure of choice is duodenotomy with local excision and frozen section to determine the histologic picture.

SARCOMA OF THE DUODENUM

Primary sarcoma of the duodenum is estimated to have an incidence of 0.003 per cent. Dixon and associates,[14] reporting 48 patients with malignant lesions of the duodenum, had 44 patients with carcinoma to 4 with sarcoma, for a comparable frequency of 11 to 1. Prey, Foster, and Dennis,[49] in a review of the literature to 1935, found only 61 authentic cases of primary duodenal sarcoma. Lymphosarcoma was noted to be four times as common as the next two, fibrosarcoma and leiomyosarcoma combined. Prey and co-workers found the average age to be 38 years with one-third of their cases under 25 years of age. Sarcoma originates in the submucosa or muscularis, grows longitudinally, infiltrating the intestinal wall and transforms the segment into a rigid nonyielding tube. Surprisingly, the lumen is rarely encroached upon sufficiently to cause

clinical obstruction prior to the growth of the mass to enormous proportions. Fungating polypoid sarcomas commonly seen elsewhere in the gastrointestinal tract are infinitely rare in this location.

Roentgenologically, sarcomas, especially lymphosarcomas, tend to show narrowing of a long, smoothed-out segment of duodenum due to destruction of the mucous membrane with obliteration of the mucosal pattern. The walls appear stiffened and without peristalsis. If only a small segment is involved, the picture may be indistinguishable from scirrhous adenocarcinoma. The treatment of choice is radical excision coupled with postoperative radiation therapy. If the tumor has spread beyond the confines of surgery, radiation has a definite palliative value.[48]

PRIMARY RETROPERITONEAL TUMORS

Primary retroperitoneal tumors, although uncommon, should not be considered rare, for Donnelly[15] in 1946 reported 95 cases from one institution and estimated that over 500 cases had been reported up to that time. Lymphosarcomas and fibrosarcomas are the most common malignant tumors, while lipomas and epithelial cysts are the most frequent benign lesions.[56] Donnelly found the average age to be 43 years, with 42 per cent under 40 years at the time of diagnosis.

Although retroperitoneal tumors are frequently mentioned as a cause of intestinal obstruction, substantiating evidence has not been found in my experience. In general, early symptoms are vague and nondiagnostic. Not until the disease is in an advanced stage does pressure on vital structures call attention to its presence. It is exceptional that such extrinsic compression leads to clinical duodenal obstruction. The treatment of choice is surgical exploration with an attempt at complete removal. Benefits derived from postoperative or palliative radiation therapy will depend upon the histology of the tumor.

PERIDUODENAL LYMPHADENOPATHY

Lymph nodes in the root of the intestinal mesentery and periduodenal region may become enlarged either from inflammatory or metastatic neoplastic processes. Pyogenic lesions such a acute appendicitis or cholecystitis have been quoted as etiological sources of lymphatic drainage resulting in extensive lymphadenopathy with duodenal obstruction.[26] Tubercular adenitis likewise has been responsible for compression of the duodenal lumen.[2] With present-day control of bovine tuberculosis, abdominal lymphadenitis due to this cause has become exceedingly rare. Careful history and physical examination should establish the primary disease process in pyogenic lymphadenitis, and proper antibiotics coupled with diligent handling of the basic condition will relieve the duodenal compression.

Extensive involvement of periduodenal nodes with metastatic carcinoma from adjacent organs has been held responsible for encroachment upon the duodenal lumen. This represents an advanced stage of malignancy and except for pancreatic carcinoma perhaps is unlikely to occur prior to recognition of the primary site of disease. Clinical symptoms of duodenal obstruction due to

extensive involvement of lymph nodes by either an inflammatory or neoplastic process is very uncommon since it represents an extrinsic form of duodenal compression and usually creates a widening of the duodenal loop with only mild encroachment upon the lumen.

INTRAMURAL HEMATOMA

This is indeed a rare clinical complication of trauma. Only two instances were found in recent English literature and both were in children. [13, 38] In each case there was a short history of epigastric pain and vomiting. Roentgenologic examination demonstrated marked narrowing of the duodenum with partial obstruction. The hematomata were evacuated through longitudinal incisions and closed transversely. Both recovered uneventfully.

GALLSTONE OBSTRUCTION OF THE DUODENUM

Gallstones as a cause of duodenal obstruction are extremely rare. Although reports in the literature indicate gallstones as responsible for 2 per cent[59] of all intestinal obstructions, at least 70 per cent lodge in the terminal ileum.[19] Hertz,[25] in a review of world literature, found 27 surgical cases with gallstones obstructing the duodenal lumen. Foss and Summers[19] noted an incidence of 0.012 per cent of gallstone obstruction of the duodenum in patients with disease of the gall bladder and biliary tract. Although uniformly accepted that large stones enter the gastrointestinal tract most frequently through erosion of the proximal duodenal wall secondary to empyema of the gall bladder, the size of the duodenal lumen is in most instances sufficient to permit passage into the smaller distal tract. If this fails to occur, the clinical picture may be confusing, for abdominal distention is not a prominent feature and visible peristalsis is rarely seen. If obstruction is complete, a rapid chain of events takes place. Shock with collapse due to extreme fluid and electrolyte loss will occur unless adequate measures are taken immediately. The exceptionally high mortality is in no small measure related to the advanced age of most patients. Disquieting observations are those of Foss and Summers[19] who reported that 15 per cent of their patients failed to give a previous history of cholecystic disease and an additional 32 per cent initially had epigastric pain suggestive of a perforating peptic process. Riesser and Vicas[52] found only 4 cases in the world literature with a correct preoperative radiographic diagnosis.

Radiographic criteria for a positive diagnosis are: (1) air or contrast media in the biliary tree, (2) direct visualization of the stone protruding or entirely within the duodenal lumen, and (3) roentgenologic evidence of obstruction proximally in the duodenum and stomach.[53] The surgical procedure of choice is to push the stone proximally into the stomach and remove it through a gastrotomy incision. If this is impossible, it may be extracted by doudenotomy. It is generally accepted that the cholecystoduodenotomy fistula closes without surgery and, if not, this residual abnormality is fully compatible with a normal life.

DUODENAL DIVERTICULUM

Perusal of the recent literature quotes duodenal obstruction as a frequent complication of duodenal diverticuli. Closer appraisal of the many fine articles,[9, 39, 44] however, fails to disclose cases of actual symptomatic duodenal occlusion. Diverticuli in this portion of the intestinal tract are by no means rare, for Cattell and Mudge,[9] in a review of several articles, found a 1.5 per cent incidence of diverticuli in upper gastrointestinal barium studies while Grant[21] reported an 11.6 per cent frequency in a large post-mortem series. The vast majority are asymptomatic, for Waugh and Johnston,[60] in a series of 525 cases, noted an incidence of only 2 per cent with symptoms demanding surgical intervention. That sufficient degrees of duodenal obstruction rarely, if ever, occur can be gathered from the 525 cases reported from the Mayo Clinic in which only two instances of duodenal obstruction were found. Both proved to be partial obstructions. Similarly, Patterson and Bromberg,[44] in a review of the literature from 1938 to 1951, mentioned no cases of significant duodenal obstruction due to diverticuli. Therefore, one must conclude that complete obstruction due to diverticuli practically never occurs, and barium studies of the duodenum should distinguish the presence of diverticuli as a cause of duodenal obstruction.

Whenever surgery is necessary, the sac is dissected from the adjacent pancreas and the neck closed by retaining a cuff of the sac to adequately obliterate the opening. Helpful adjuncts which reduce the risk to adjacent structures are freeing the duodenum by the Kocher maneuver, catheterization of the common bile duct, and dissection of the wall of the sac with a finger inserted in the lumen of the diverticulum as advocated by MacLean.[34]

SUMMARY

The causes of postbulbar duodenal obstruction have been reviewed. The relative frequency, symptomatology, roentgenologic findings, and mode of treatment of each condition have been discussed.

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Appraisal of Progress in Surgical Therapy

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INFLAMMATORY CARCINOMA OF THE BREAST: A CRITIQUE OF THERAPY

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INFLAMMATORY carcinoma of the breast is considered categorically inoperable by Haagensen and Stout[3, 4] Other authors[2, 6, 8] deprecate surgical intervention, or advocate only nonoperative measures in this type of cancer. An analysis of the data given in the literature reveals insufficient evidence either to support such a contention or to reject it. We have studied the problem by analyzing the experience of the Hospital of the University of Pennsylvania over a twenty-six-year period ending June 30, 1952.

MATERIAL

During this twenty-six-year period 1,774 patients were treated for pathologically proved carcinoma of the breast. Of these, 46, or 2.6 per cent, had primary inflammatory carcinoma of the breast. All of the 46 demonstrated the skin manifestations of erythema, edema, peau d'orange, and increased local heat. Those patients who had the cutaneous signs of inflammation over only a localized area at the site of skin attachment and those in whom the signs of inflammation were thought to be caused by the bacterial invasion of a cancer were excluded from the study. Patients who developed inflammatory recurrences of carcinoma following operation are not included in the study.

CLINICAL DATA

One of the patients was a man; the other forty-five were women. Thirty-three were white and fourteen Negro, a race incidence similar to that of our entire group of patients with breast cancer. The age range was from 26 to 80 years, with an arithmetic mean age of 49.9 years. Fifty per cent of the women

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were postmenopausal. None were pregnant but one was lactating. The pretreatment duration of the inflammatory signs ranged from ten days to twelve months.

A majority of the patients had a diffusely enlarged breast. Thirty per cent either had cancer of both breasts on admission or later developed cancer of the second breast. Fifteen per cent had a nipple discharge. The rapid spread of this type of cancer is shown by the finding that 95 per cent had axillary metastases and 43 per cent had supraclavicular metastases at the time of initial examination.

TREATMENT

The methods of treatment were: x-ray radiation for 24 patients; radical mastectomy for 10 patients; simple mastectomy for 10 patients; estrogen therapy for one patient; and no therapy for one patient. With one exception, all of the patients who had a radical mastectomy received postoperative irradiation, and all but one of the patients who had a simple mastectomy received postoperative irradiation. One of the patients who had a radical mastectomy and five of the patients who had a simple mastectomy were given preoperative irradiation. Many of the patients were treated with hormones during the terminal stages of their disease.

RESULTS

The results of treatment are tabulated in Table I. One patient is alive and free of disease eight years after radical mastectomy. Another patient, treated by x-ray radiation alone, has lived seven years since the beginning of treatment. Both breasts and a large portion of the anterior chest wall are involved with cancer at the present time but no distant metastases are demonstrable. All of the other patients are dead. Sixty per cent died within one year, 80 per cent within two years, and over 90 per cent within three years. One third of those treated primarily with irradiation were dead within six months or less. One death occurred, within six months, in the group with radical mastectomy, and one in the group with simple mastectomy.

TABLE I. SURVIVALS AFTER INITIATION OF TREATMENT

TREATMENT	NUMBER PATIENTS	PER CENT SURVIVING AT:					
		6 MONTHS	12 MONTHS	18 MONTHS	2 YEARS	3 YEARS	5 YEARS
X-ray	24	67	33	25	17	8	4
Simple mastectomy	10	90	40	30	10	0	-
Radical mastectomy	10	90	60	40	40	10	10
Estrogens only	1	100	0	-	-	-	-
No therapy	1	0	-	-	-	-	-
Totals	46	76	39	28	20	7	4

As the patients with more advanced disease are thought to have been more likely treated primarily by irradiation, the data have been broken down to include only those patients without evident supraclavicular and distant metastases and in whom the skin involvement did not extend beyond reasonable lines of

resection. Twenty-four of the forty-six patients met these criteria. Data concerning their treatment and survival are presented in Table II. Little difference exists in the survival rate between the group treated by radical mastectomy and the group treated primarily by irradiation. No matter what the form of treatment, the survival was poor. Of the entire group, one-half survived eighteen months, one third two years, and less than 10 per cent for five years. The radical mastectomy group is small but the results are similar to a larger series reported by Meyer and associates,[7] and are slightly better than the results of other forms of treatment.

TABLE II. SURVIVALS AFTER INITIATION OF TREATMENT

PRIMARY TREATMENT	NUMBER PATIENTS	PER CENT SURVIVING AT:				
		1 YEAR	18 MONTHS	2 YEARS	3 YEARS	5 YEARS
X-ray	11	64	45	27	18	9
Simple mastectomy	6	33	33	17	0	0
Radical mastectomy	7	71	71	57	14	14
Totals	24	58	50	33	12.5	8

DISCUSSION

Inflammatory carcinoma of the breast comprises about 2 per cent of all carcinoma of the breast. The primary type of inflammatory carcinoma typically is manifested by a diffusely enlarged painful breast with erythema, edema, peau d'orange, and increased local heat. A palpable mass may or may not be present. When the patient is first examined the cancer has usually spread to the axillary nodes and often to the supraclavicular nodes and more distant sites. The rate of growth is often startling, and may fill the breast within a matter of weeks. The lesion is often misdiagnosed and mistreated as a nonmalignant inflammatory process.

The best means of treating inflammatory carcinoma of the breast is unknown. The course of the disease often has been a rapidly fatal one, regardless of the type of therapy. Lee and Tannenbaum[6] reported a series of 28 patients in whom surgical and nonsurgical treatment was compared. They emphasized the rapid downhill course of some of the patients following operation and concluded that inflammatory carcinoma "is a distinct clinical group in the field of mammary carcinoma in which all cases do badly if treated surgically." This article has been quoted widely in the literature and in our own clinic as evidence against surgical intervention in all patients with inflammatory carcinoma. Yet the data in the article are insufficient to support such a conclusion. Their data show equally poor results in those patients treated only by nonoperative means. At the time reported, many of the patients treated by nonoperative means had died less than six months after initiation of treatment.

The high recurrence rate following operation has been used as an argument against surgery. Our recurrence rate was 50 per cent, as was that of Haagensen and Stout[3] and Meyer and associates.[7] On the other hand, in patients treated nonoperatively there may be a local persistence of the tumor

mass from beginning to death. In our series, this locally disseminated neoplasm often ulcerated, became painful, and sometimes spread widely and rapidly even during a course of x-ray radiation.

No evidence exists in our series or in the larger series of Meyer and associates[7] that surgical intervention accelerates the course of the disease. Nor are data available in the literature which show significantly better results following palliative measures. The only previously reported five-year survivals that we have found have all had radical mastectomy.[1, 5, 7] Our one five-year survival following irradiation alone is alive at this writing, but has an extensive, ulcerated, cancer which has involved the opposite breast and a large portion of the chest wall.

We do not contend that our data or those in the literature show significantly better results with operation than with nonoperative methods. It seems probable that the disease is so highly lethal that the best method of treatment will be hard to prove on the small samples now available for analysis. We believe that the widespread teaching that operation is contraindicated for all patients with inflammatory carcinoma of the breast is untenable. In many of these patients the disease will have obviously spread past the limits of surgical removal. In others, however, the disease may be more limited and operation should not be denied the patient merely because limited inflammatory signs are present.

SUMMARY AND CONCLUSIONS

A series of 46 patients with primary inflammatory carcinoma of the breast is reported. The patients have been analyzed according to the principal method of treatment.

Many authors have considered inflammatory carcinoma of the breast inoperable, and state that surgical intervention accelerates the dissemination of the disease. Our data, and the data reported in the literature are insufficient to support this hypothesis or to reject it. The disease is usually highly lethal no matter what form of treatment is given.

Our series includes one patient alive and well eight years following a radical mastectomy. The only other previously reported five-year survivals have all had a radical mastectomy.

We believe that radical mastectomy is justified in selected patients with inflammatory carcinoma of the breast in whom there is no evidence of extension of the carcinoma beyond the confines of a reasonable radical mastectomy.

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Book Reviews

The Postural Complex. By Laurence Jones. Pp. 156. Springfield, 1954, Charles C Thomas, Publisher.

This book deals with the relation of posture to the neuralgic pain in various parts of the body, such as cervical neuralgia, thoracic radiculitis, low-back pain, sciatica, and foot and leg pains. The cause of these complaints is attributed to an almost universal rotatory deviation in the feet and legs which has been found by the author in his patients. The book is devoted to an exhaustive explanation of the method of detecting these deviations. The author treats these symptoms by means of specially devised shoe corrections and obtains excellent results. If other physicians can attain the same results by these methods of treatment, this little monograph may revolutionize the treatment of these complaints. Otherwise, it will be relegated to the shelf of medical curiosities. The latter fate is most probable.

The History and Conquest of Common Diseases. By Walter R. Bett. Pp. 334. Norman, Oklahoma, 1954, University of Oklahoma Press.

This monograph on *The History and Conquest of Common Diseases* should be read by every thoughtful physician. It is an ideal bedside book as it can be devoured piecemeal, chapter by chapter, without losing its impact. The documentation and bibliographies are excellent. The book is written in a manner simple enough to be meaningful to the informed layman and, at the same time, it is technical enough to satisfy the demands of the practitioner. One of the most interesting chapters is the one entitled "Malingering," since this is a subject with which most physicians are generally unacquainted. With a high literary standard and a broad appeal, this book should have a wide circulation.

Intestinal Obstruction. Physiological, Pathological and Clinical Consideration With Emphasis on Therapy Including Description of Operative Procedures. By Owen H. Wangensteen. Ed. 3. Springfield, Ill., 1955, Charles C Thomas, Publisher.

This monograph, which started in the first edition as a very small book and which included primarily the use of the Wangensteen suction, has developed into an encyclopedia. It is without a doubt the most complete discourse on the subject of intestinal obstruction that is available. As stated in the preface, the book is more mature than its predecessors, which is indeed true. It represents the lifework of a team of extremely active workers, headed by a genius with a very active and imaginative mind. Embodied in the work are the results of many investigations performed by the University of Minnesota Surgical Staff under Dr. Wangensteen's leadership.

An important part of the present volume is a careful analysis of 1,252 cases of acute mechanical obstruction observed at the University of Minnesota Hospital from Jan. 1, 1942 to Sept. 1, 1953. Thirty-one per cent of these were due to adhesions, of which 24.6 per cent were postoperative, and 6.4 per cent were primary adhesions. Twenty-seven and four-tenths per cent were due to neoplasms, of which 16.6 per cent were due to primary lesions and 10.8 per cent were due to carcinosis. Ten and four-tenths per cent were due to external hernias. The remainder were due to miscellaneous causes, such as

operative complications (8.69 per cent), inflammatory strictures (3.8 per cent), imperforate anus (3.4 per cent), volvulus (3.4 per cent), megacolon (3.3 per cent), and intussusception (2.8 per cent).

Considerable emphasis is placed upon the recognition of intestinal obstruction both clinically and by laboratory methods. A great deal of emphasis is placed upon the treatment of acute intestinal obstruction, including adjuvant measures, such as fluid and electrolyte replacement, use of tube suction with description and evaluation of the various types of tubes employed. As the author states in his introduction, less emphasis is placed upon tube drainage than previously. Whereas in the past twenty-four years 12 patients have died with intestinal gangrene or other complications of delay because of tube drainage, during the past four years only 4 patients have died. The various methods which favor the introduction of tubes through the pylorus are described, particularly that of Grafton Smith, which was developed and is being used at the University of Minnesota.

The operative treatment of intestinal obstruction is thoroughly covered, including the author's method of decompression suction enterotomy and the types of aspetic resection which he has elaborated so well. There is a complete chapter on the postoperative treatment of the patient who has had intestinal obstruction, which is followed by a complete chapter on the mortality of acute intestinal obstruction.

Approximately half the book is concerned with a consideration of special types of intestinal obstruction, such as congenital lesions, benign and malignant strictures of the bowel; and, as might easily be imagined, a great deal of emphasis is placed on the "second look" operations for carcinoma of the large bowel. With the evidence presented, there can be no doubt about the validity of this precedure. Intraluminal obstructions are also considered. Megacolon, compression of the bowel from without, obstruction due to adhesions, functional ileus, intestinal obstruction due to external and internal hernias, volvulus, intussusception, obstruction due to anomalies of rotation, adynamic and spastic ileus, those due to vascular causes, such as mesenteric thrombosis and embolism, are considered extensively.

As mentioned previously this monograph is an encyclopedia of information concerning intestinal obstruction and should be in the library of every physician whether he is interested in surgery or internal medicine.

The Battle for Mental Health. By James Clark Moloney. Pp. 105. New York, 1952, Philosophical Library. $3.50.

This little volume was written ostensibly to impress the layman with the enormous problem of mental ill-health and to suggest methods of prevention. In both purposes it seems to have failed.

The author, who is announced by the publishers as an eminent American psychoanalyst is a member of the Cornelian Corner group in Detroit. This volume is presented as an exposition of the doctrines and beliefs of this group. Most of the mental ills of the present day he attributes to harmful influences of the first few days of life. By inference, the reader is led to believe that if the newborn were left with the mother rather than kept in a nursery, most of the mental disturbances of later life would be avoided.

The reviewer, who is not a psychiatrist, finds the book strangely unconvincing even though the publishers claim that "Dr. Moloney supports his theories with scientific clinical, anthropological, and experimental observations." The reader will search in vain for factually supported data. Rather will he find sweeping generalizations. The bottle-fed baby is portrayed as having "had no warm, interpersonal relationship with his mother" at the head end, yet "at the other end. . . . . a warm relationship. . . . . for it was customary for her to cleanse the baby's buttocks with one hand as she held the baby's feet up with the other hand. . . . . Therefore, at the buttocks, genital or anal end, a type of direct experience with the mother took place which had no counter-

part at the mouth or head-end'' with the result that ''the baby subsequently surrendered the mouth end of his body as a site for love in favor of the anal end which was more considerately treated.'' One wonders if Dr. Moloney ever saw a mother kiss a baby on the head or neck.

His attack on obstetrical practices is ill-tempered and emotional. The reviewer cannot agree that obstetricians, pediatricians and maternity nurses are motivated by ''their inner needs to secure these roles for neurotic self-fulfillment,'' that ''efficient, childless women as supervisors dominate nurseries'' or that obstetricians are ''intellectual stopcocks to social progress'' who through their ''unconscious conspiracy with maternity and hospital nurses, their unconscious collusion with hospital management'' have ''undermined the gains made in the field of infant mortality and maternal mortality.''

Emotional outbursts of this type are not designed to convince the lay reader of the critical judgment of the author or the soundness of the doctrines that he preaches. It is unfortunate that a problem so important for society and a new approach so potentially helpful does not find a more temperate and convincing champion.

Transplantation of Tissue, Vol. 1. By Lyndon A. Peer. Pp. 421. Baltimore, Md., Williams & Wilkins Company.

Volume 1 of this book considers transplantation of cartilage, bone, fascia, and tendon and muscle. Each subject is generally considered with a review of first, animal experiments and their results; second, human transplants and their success; and last, the clinical applications of the use of the graphs in the more technical features. As would be anticipated in a book of this nature, which is largely a review of the literature, the bibliographies are extensive. Unfortunately, they have not been placed in alphabetical order and there is some repetition and duplication of the references in portions of the bibliography. A little more activity on the part of the editor in organizing these bibliographies would have increased the value of the work tremendously. It is hoped that subsequent volumes will correct this deficiency. These volumes as judged by the initial venture will be of particular value to surgeons engaged in the work of the experimental laboratory as they provide a tremendous quantity of background and historical information. This initial volume is particularly valuable for plastic surgeons because of its discussion of cartilage transplants, and to orthopedic surgeons because of the material on bone, fascia, and muscle.

Neck Dissections. By James Barrett Brown and Frank McDowell. Pp. 163. Springfield, Illinois, 1954, Charles C Thomas, Publisher.

Neck Dissections is a monograph in the Bannerstone Division of American Lectures in Surgery. The authors discuss preoperative considerations, postoperative care, and the operative techniques of neck dissection alone and in combination with resection of the primary tumor.

In the first chapter the difficulties and errors in clinical and microscopic diagnosis of neck metastases, the effectiveness of block dissections in curing metastatic neck cancer, and the resistance of metastatic neck cancer to radiation are enumerated. Doctors Brown and McDowell suggest that the term ''prophylactic dissection'' be abandoned in favor of the phrase ''dissection for probable small metastases'' when referring to neck dissections, especially in patients with carcinoma of the lip.

The actual technique of neck dissections is described in detail, and eleven full color drawings plus eleven black and white drawings add greatly to the clarity of the presentation. The use of Kirschner wire for stabilization of jaw fragments in patients undergoing neck dissection and jaw resection is illustrated, and the routine use of tracheotomy in such patients is decried.

This monograph is more than a manual on operative technique, for it covers medical and surgical considerations in patients who are candidates for neck dissections.

Calendar of Surgical Meetings

THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY. *Annual Meeting*, Nov. 1-3, 1956, Camel Back Inn, Phoenix, Ariz. Secretary, Eben Alexander, Jr., M.D., Bowman Gray School of Medicine, Winston-Salem, N. C.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS. *Annual Meeting*, June 4-6, 1956, Oyster Harbor Hotel, Osterville, Mass. Deadline for papers, Feb. 10, 1956. Secretary, John A. Taylor, M.D., 2 East 54th St., New York, N. Y.

AMERICAN ASSOCIATION FOR THE SURGERY OF TRAUMA. *Annual Meeting*, Oct. 4-6, 1956, The Biltmore, Santa Barbara, Calif. Deadline for papers, July 1, 1956. Secretary, James K. Stack, M.D., 700 N. Michigan Ave., Chicago 11, Ill.

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY. *Annual Meeting*, May 7-9, 1956, Hotel Fontainebleau, Miami Beach, Fla. Secretary, Paul C. Samson, M.D., 3959 Happy Valley Rd., Lafayette, Calif.

AMERICAN CANCER SOCIETY, INC. *Third National Cancer Conference*, June 4-6, 1956, Sheraton Cadillac Hotel, Detroit, Mich. Coordinator, Brewster S. Miller, M.D., 521 West 57th St., New York 19, N. Y.

AMERICAN COLLEGE OF SURGEONS. *Sectional Meetings*, 1956: Jan. 16-18, Hotel George Washington, Jacksonville, Fla.; Feb. 13-16, The Bellevue-Stratford, Philadelphia, Pa.; Feb. 27-29, Hotel Schroeder, Milwaukee, Wis.; March 5-7, The Broadmoor, Colorado Springs, Colo.; March 12 and 13, Hotel Marion, Little Rock, Ark.; April 23-25, The Macdonald, Edmonton, Alberta. *Clinical Congress*, Oct. 8-12, Civic Auditorium, San Francisco, Calif. Secretary of the College, Michael L. Mason, M.D., 154 E. Erie St., Chicago 11, Ill.

AMERICAN GYNECOLOGICAL SOCIETY. *Annual Meeting*, May 21-23, 1956, The Shoreham, Washington, D. C. Secretary, John I. Brewer, M.D., 104 S. Michigan Avenue, Chicago, Ill.

AMERICAN MEDICAL ASSOCIATION. *Annual Meeting*, June 11-15, 1956, headquarters, Navy Pier, Chicago, Ill. *Clinical Session*, Nov. 27-30, 1956, Civic Auditorium, Seattle, Wash. Deadline for papers, Aug. 1, 1956. Secretary, Council on Scientific Assembly, A. M. A., 535 N. Dearborn St., Chicago 10, Ill.

THE AMERICAN ORTHOPAEDIC ASSOCIATION. *Annual Meeting*, June 16-20, 1956, Banff Springs Hotel, Banff, Alberta. Secretary, George O. Eaton, M.D., 4 East Madison Ave., Baltimore, Md.

THE AMERICAN SURGICAL ASSOCIATION. *Annual Meeting*, April 11-13, 1956, The Greenbrier, White Sulphur Springs, W. Va. Secretary, R. K. Gilchrist, M.D., 59 East Madison St., Chicago 3, Ill.

AMERICAN UROLOGICAL ASSOCIATION. *Annual Meeting*, May 28-31, 1956, Statler Hotel, Boston, Mass. Secretary, Samuel L. Raines, M.D., 188 S. Bellevue Blvd., Memphis, Tenn.

THE CENTRAL SURGICAL ASSOCIATION. *Annual Meeting*, Feb. 23-25, 1956, Kahler Hotel, Rochester, Minn. Secretary, Charles D. Branch, M.D., 102 North Street, Peoria, Ill.

THE HARVEY CUSHING SOCIETY. *Annual Meeting*, April 16-18, 1956, Reef Hotel, Honolulu, Hawaii. Secretary, David L. Reeves, M.D., 316 West Junipero St., Santa Barbara, Calif.

NEW ENGLAND SURGICAL SOCIETY. *Annual Meeting*, Oct. 5 and 6, 1956, Poland Springs House, Poland Springs, Maine. Deadline for papers, June 1, 1956. Secretary, Richard Warren, M.D., Peter Bent Brigham Hospital, 721 Huntington Avenue, Boston 15, Mass.

SOCIETY OF NEUROLOGICAL SURGEONS. *Annual Meeting*, May 7 and 8, Memphis, Tenn. Secretary, Bronson S. Ray, 525 E. 68th St., New York, N. Y.

THE SOCIETY OF UNIVERSITY SURGEONS. *Annual Meeting*, Feb. 9-11, 1956, Claypool Hotel, Indianapolis, Ind. Secretary, C. Rollins Hanlon, M.D., 1325 S. Grand, St. Louis, Mo.

THE SOCIETY FOR VASCULAR SURGERY. *Annual Meeting*, June 10, 1956, The Conrad Hilton, Chicago, Ill. Deadline for papers, March 15, 1956. Secretary, Henry Swan, M.D., 4200 E. 9th Ave., Denver, Colo.

SOUTHERN SURGICAL ASSOCIATION. *Annual Meeting*, Dec. 4-6, 1956. Deadline for papers, Sept. 20, 1956. Secretary, George G. Finney, M.D., 2947 St. Paul St., Baltimore, Md.